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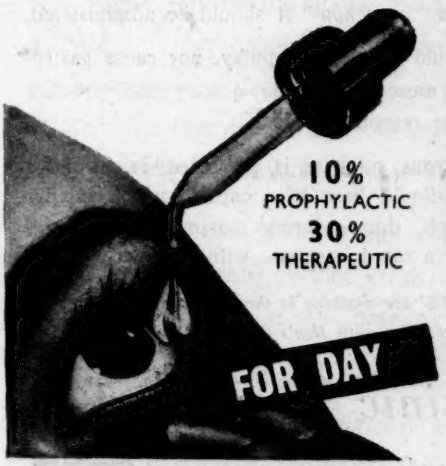

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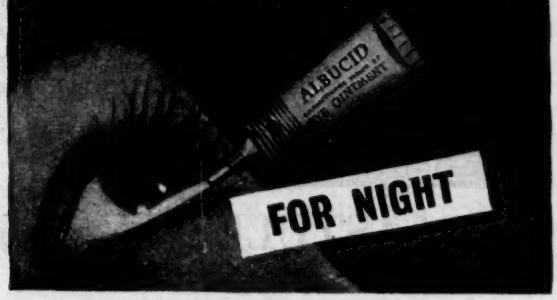

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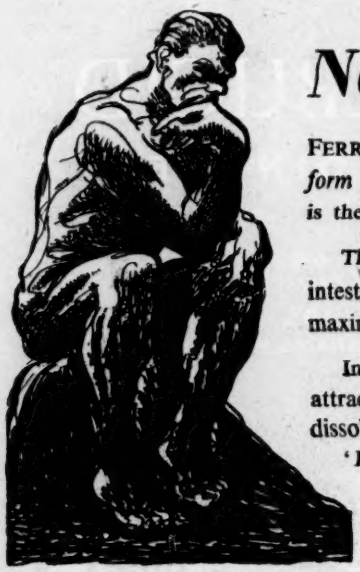

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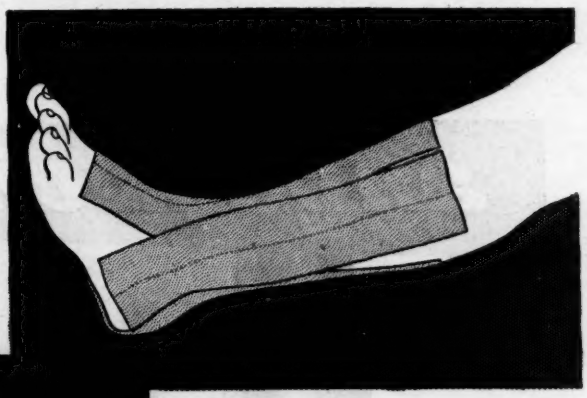

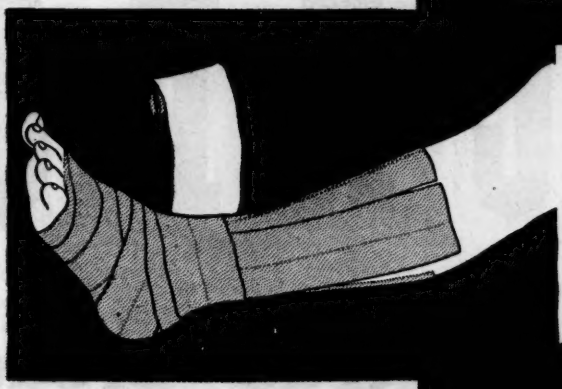

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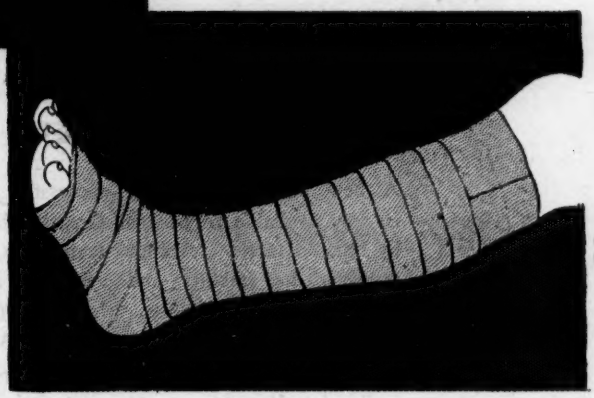
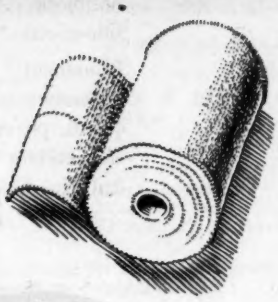
Vertical strips—enclosure of heel—even overlapping—no creases—firm and even pressure, are some of the important points in technique.



Elastoplast

TRADE MARK

POROUS ADHESIVE BANDAGES B.P.C.



The Elastoplast Bandage with Porous Adhesive complies with the B.P.C. It provides firm adhesion, compression and support while permitting free evaporation of skin exudates. Full details from Smith & Nephew Ltd., Welwyn Garden City, Herts., the marketing organisation of T. J. Smith & Nephew Ltd., Hull.

OUTSIDE THE BRITISH COMMONWEALTH ELASTOPLAST IS KNOWN AS TENSOPLAST

announcing Achro

the true broad s

A new and outstandingly successful antibiotic—ACHROMYCIN Tetracycline—is now available for use in Great Britain and overseas countries. Developed by the Lederle research team, ACHROMYCIN is outstanding in many respects. Its stability and solubility surpass those of any broad-spectrum antibiotic in current use. Moreover, no case has yet been reported of the development of bacterial resistance to ACHROMYCIN.

The antibacterial range of ACHROMYCIN is as great as that of any known antibiotic. Yet this new drug shows a remarkable freedom from undesirable side-effects.

Prominent among the many indications for ACHROMYCIN are beta haemolytic streptococcal infections, *E. coli* infections, meningococcal, staphylococcal, pneumococcal and gonococcal infections; acute bronchitis, bronchiolitis and certain mixed infections. Recommended basic adult dosage is 1 Gm. *daily in divided doses—by mouth or injection.*

Lederle

LEDERLE LABORATORIES DIVISION

omycin*

HYDROCHLORIDE TETRACYCLINE HCl

Lederle

spectrum antibiotic

- More Rapid Absorption
- Fewer Side-Effects
- Greater Stability

Achromycin is at present only available to hospitals.

CAPSULES: 50-mg.—vials of 25 and 100
250 mg.—vials of 16 and 100

INTRAVENOUS: Vials of 250 mg. and 500 mg.

SPERSOIDS†: *Dispersible Powder;* Jars of 36 Gm. and 75 Gm. Each teaspoonful (3.0 Gm.) contains 50 mg. of Achromycin Tetracycline.

Other dosage forms are being developed as rapidly as research permits.

*Regd. Trade Mark †Trade Mark

Cyanamid Products Ltd. BUSH HOUSE · ALDWYCH · LONDON, W.C.2 · TEMPLE BAR 5411

. . . give great faith in these Dalmas Tulle Gras Dressings

DALMAS TULLE GRAS DRESSINGS

SULPHONET

Wide mesh gauze impregnated with petroleum jelly, balsam of peru, and sulphathiazole 5%. A ready-to-use sterile dressing for wounds, burns, skin grafts and areas where there has been skin loss.

In squares 3½" x 3½" and strips 5 yds. x 3½". Packed singly and in boxes of 5, 10 and 36 dressings. Available on E.C.10.

PETRONET
(Paraffin Gauze Dressing, B.P.C.)

A sterile dressing impregnated with petroleum jelly and balsam of peru. For all lesions, abrasions, ulcers; these dressings ensure painless removal.

In squares 3½" x 3½" and packed singly and in boxes of dressings 5, 10 and 36. Also in strips of 8 yds. x 3½". Available on E.C.10.

URO-SULPHONET

A strip dressing impregnated with a wool alcohol emulsion containing Sulphathiazole 5% and Urethane 2%. Provides a dressing that is bacteriostatic and analgesic; destroys offensive wound odour. Also an ideal burn dressing. Packed in a continuous strip 3½" x 5 yds.

DALMAS

M4

DALMAS LIMITED, LEICESTER & LONDON. Established 1823

'. . . the presence of disease upon the surface of the skin *is a source of great mental distress to the patient. It is ever in his consciousness, setting him apart from his fellows . . .'**

Practitioner* (1954) **172, 55

to the acne patient
'ESKAMEL' brings great improvement

within a short time ; it also masks the lesions meanwhile.
'Eskamel' caters for *both* aspects of acne treatment

For cost to N.H.S., please see M. & J. list of costs dated April, 1954

MENLEY & JAMES, LIMITED, COLDHARBOUR LANE, LONDON, S.E.5

EMF64 for *Smith Kline & French International Co., owner of the trade mark 'Eskamel'*

November 1, 1954

AUREOMYCIN

CHLORTETRACYCLINE, *Lederle*

derestricted

As from Monday November 1, 1954, the restrictions imposed by the Ministry of Health, limiting the supply of AUREOMYCIN (Chlortetracycline) Hydrochloride Crystalline *Lederle* to hospitals, are completely removed. As from that date doctors are free to prescribe AUREOMYCIN in general practice whenever required for private or National Health Service patients without restrictions. AUREOMYCIN is manufactured in the United Kingdom and is in adequate supply for doctors and hospitals.

AUREOMYCIN (Chlortetracycline) is the original broad-spectrum antibiotic which combines potency with safety and economy. More reports have appeared on the excellent clinical results with AUREOMYCIN than any other broad-spectrum antibiotic. There is a form of AUREOMYCIN for every purpose.

Capsules	Ophthalmic Ointment	Spersoids*
Dental Cones	Ophthalmic	*Dispersible Powder*
Dental Paste	Oral Drops	Syrup
Intravenous‡	Otic	Troches
Nasal	Soluble Tablets	Vaginal Powder
Ointment		

‡At present available to hospitals only.
* *Trade Mark*

Can be prescribed on N.H.S. Form E.C.10

AUREOMYCIN ***means greater action . . smaller dosage . . lower cost***

LOOK TO *Lederle* FOR LEADERSHIP

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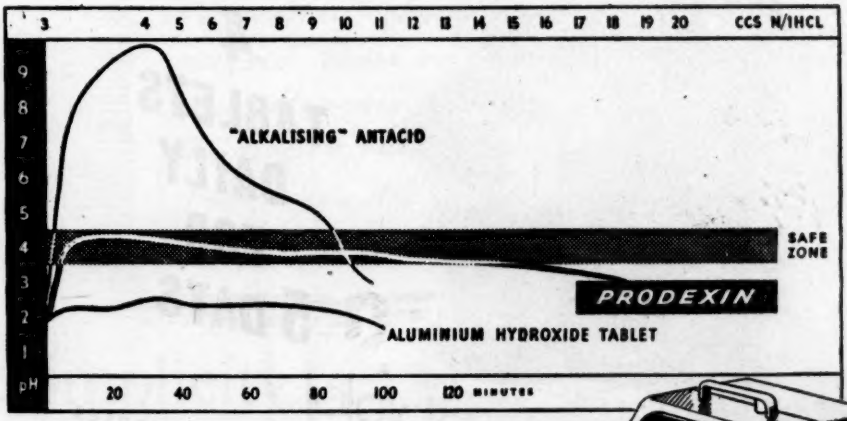
16

A New development providing CONTROLLED antacid therapy

Prodexin is a new product containing aluminium glycinate, and belongs to the buffer group of antacids. It depends for its action upon the slow release, on hydrolysis, of active aluminium hydroxide gel and glycine (amino acetic acid). Glycine rapidly raises the pH to 2, sparing the aluminium gel for the later stage of raising it into the "safe zone" of pH 3·5 to 4·5. Prodexin maintains an equable gastric environment for long periods without alkalisation.


3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 CCS N/1HCL
9 8 7 6 5 4 3 2 1 pH
"ALKALISING" ANTACID
SAFE ZONE
PRODEXIN
ALUMINIUM HYDROXIDE TABLET
20 40 60 80 100 120 MINUTES

Prodexin provides a convenient, economical and safe treatment for HYPERACIDITY and PEPTIC ULCER.

The tablets, sucked one at a time, maintain the pH of the stomach contents within the "safe zone" for up to two hours. With Prodexin there is no risk of acid rebound or alkalosis. Prodexin tablets are pleasant to suck and they do not form gritty particles in the mouth or give rise to constipation.

PRODEXIN

Each tablet contains:—

Aluminium glycinate.....0·9 gramme.
(*dihydroxy aluminium aminoacetate*)

Light magnesium carbonate.....0·1 gramme.

The basic N.H.S. cost of treatment at the rate of 6 Prodexin tablets daily is 8½d.

Manufactured in the laboratories of

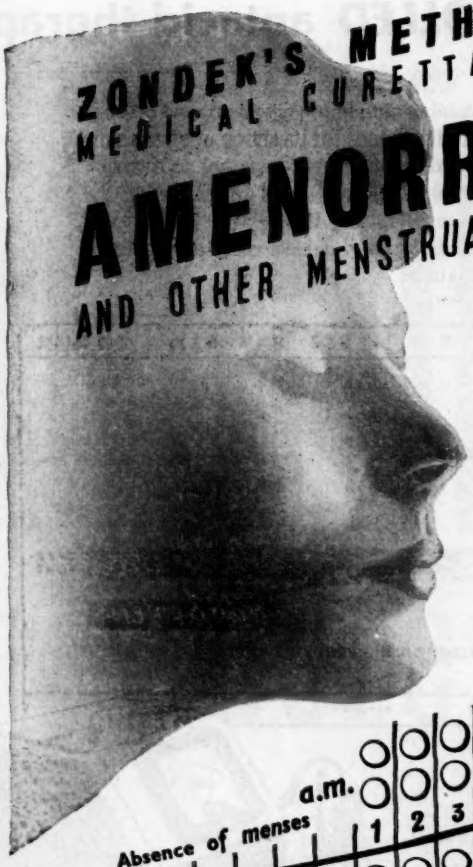
C. L. BENCARD LIMITED

MINERVA ROAD · PARK ROYAL · LONDON N.W.10

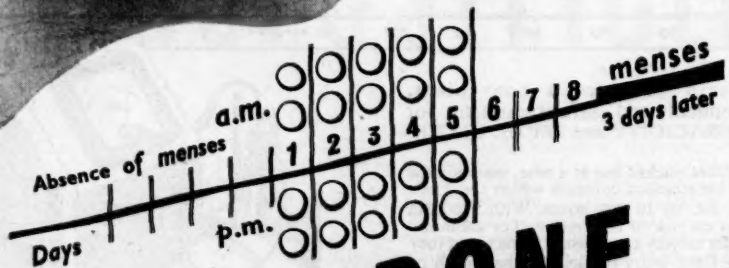
BENCARD

ZONDEK'S METHOD
MEDICAL CURETTAGE

AMENORRHOEA
AND OTHER MENSTRUAL DISORDERS



4
TABLETS
DAILY
FOR
5 DAYS

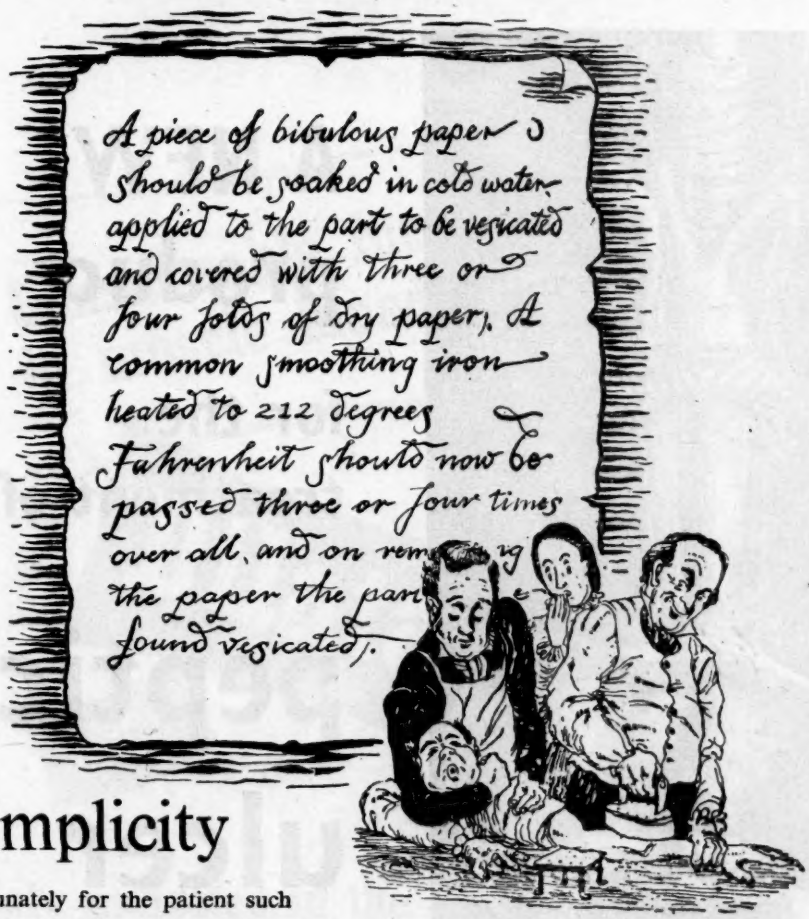


AMENORONE

Each Tablet contains Ethisterone 10 mg. Ethinyl Oestradiol 0.01 mg.
Box of 20 Tablets intended for a 5-day course
BASIC N.H.S. COST 9/6

ROUSSEL

843-847 Harrow Road,
London, N.W.10.
LADbroke 3608


A piece of bibulous paper
should be soaked in cold water
applied to the part to be vesicated
and covered with three or
four folds of dry paper. A
common smoothing iron
heated to 212 degrees
Fahrenheit should now be
passed three or four times
over all, and on removing
the paper the part
found vesicated.

Simplicity

Fortunately for the patient such primitive procedures have passed into oblivion; but the basic principles of counter-irritation still remain.

ALGIPAN Balm is the modern physiological outlet for the rubefacient treatment of non-articular rheumatism. Application of this smooth, clean, histamine cream by the patient is *simplicity* itself.

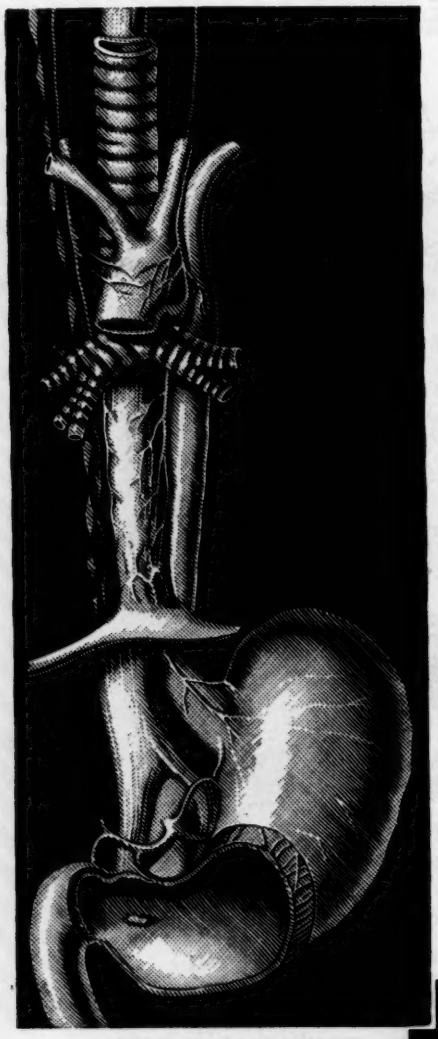
ALGIPAN is non-greasy, will not stain or damage clothes, has no objectionable odour, and is harmless to the most sensitive skin.

ALGIPAN is available in 40 G. tubes. Convenient for the ambulant patient.

Wyeth

JOHN WYETH & BROTHER LIMITED
Clifton House, Euston Road, London, N.W.1.

'Algipan'
Trade Mark
BALM



A NEW product for the treatment of peptic ulcer

MONODRAL

Trade Mark

By its powerful retarding effect on gastric motility, 'Monodral'* brings rest to the injured tissues thus relieving severe ulcer pain and helping to produce favourable conditions for healing. 'Monodral' also reduces acid secretion, is well tolerated and may be successfully combined with antacid therapy. Available in small, easy to take "caplets" containing 5 mg. active principle. Medical literature and a trial supply will gladly be sent on request.

BAYER PRODUCTS LTD
AFRICA HOUSE
KINGSWAY, LONDON W.C.2

Associated export company: Winthrop Products Ltd., London

* *2-diethylaminomethyl-2-cyclopentyl-2-(2-thienyl) hydroxyacetate methobromide*

Considerable increase in muscle blood flow

Dilatal
TRADE MARK

low toxicity

Widely indicated in the treatment of circulatory disorders

- INCREASED CARDIAC OUTPUT MAINTAINS MEAN ARTERIAL PRESSURE.
- DIRECT ACTION ON THE MUSCULATURE OF THE BLOOD VESSELS.

DILATAL* is safe and rapidly effective by oral and parenteral administration. Available in tablets (2.5 mg. in containers of 100 and 500) and ampoules (5 mg. in 1 ml.—in boxes of 12).

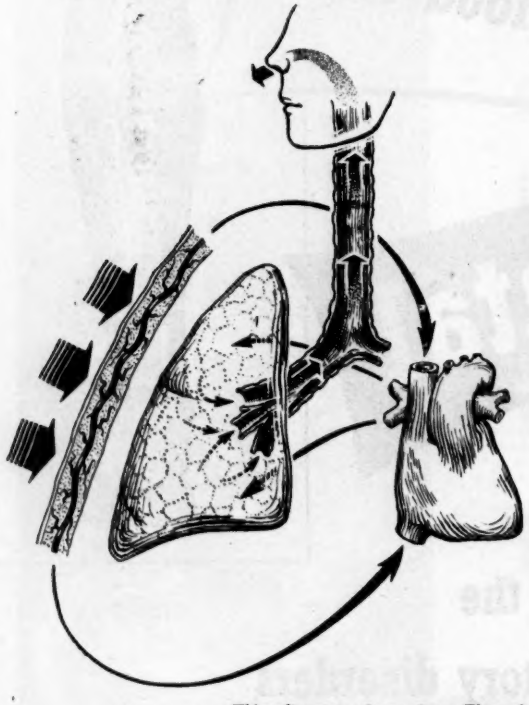
* 1-(p-hydroxyphenyl)-2-(1'-methyl-3'-phenyl-propylamino)-propanol-(1) hydrochloride

SMITH & NEPHEW LTD.,
WELWYN GARDEN CITY, HERTS.,
the marketing organisation of Herts Pharmaceuticals Ltd.,
the manufacturers and owners of the trade mark DILATAL.

GM160

A NEW ADJUVANT IN THE TREATMENT OF RESPIRATORY DISORDERS

Lloyd-Hamol Ltd., of London and Zurich, announce the launching in this country of Thoracin, a new decongestive salve for the symptomatic relief of coughs, colds and respiratory disorders.



This diagram shows how Thoracin components penetrate the skin, are carried by the bloodstream to the alveoli and excreted there to exert their effect

▶ The Thoracin formula is based on the same principles that have made Transvasin so successful in the treatment of rheumatic conditions.

▶ Thoracin is composed of esters of substituted hydroxy aromatic derivatives.

▶ Thoracin achieves the effect of the classic counter-irritant remedies — poultices, plasters and cupping — without irritation of the skin.

▶ Thoracin contains a new ester of Guaiacol that is entirely free from the evil smell and irritant effect associated with this phenol derivative in its pure form. This ester easily penetrates the skin, and is excreted in the alveoli, where it exerts its well-known action.

▶ Thoracin ensures vasodilation of the superficial skin vessels by the use of esters of nicotinic acid.

▶ Thoracin relieves reflex spasm of the pectoral muscles by the use of the tetrahydrofurfuryl-ester of salicylic acid.

▶ Thoracin brings to the alveoli via the blood stream the sedative, antispasmodic, and expectorant properties of camphor and eucalyptus.

THORACIN is available in 1 oz. tubes — basic price 2/6 plus 7½d. P.T. It is an ethical product, and is not advertised to the public. Since a very small quantity is sufficient for each application, the cost of treatment is extremely low. *Samples and literature will be gladly sent on application.*

FORMULA

Phenyl Ethyl Nicotinate	2.0%w/w
Guaiacol Furoate	5.0%w/w
Tetrahydrofurfuryl Salicylate	10.0%w/w
Camphor	3.0%w/w
Eucalyptol	2.0%w/w
Water-Miscible Base to	100.0%

LLOYD-HAMOL LTD.
11 WATERLOO PLACE, LONDON S.W.1
AND AT ZURICH

THORACIN

MADE BY THE MANUFACTURERS OF TRANSVASIN

TOLSERAM

MEPHENESIN CARBAMATE

The new SQUIBB product

for the treatment of–

***MUSCLE SPASM (including fibrositis)**

***CERTAIN NEUROLOGICAL DISORDERS**

The results of extensive clinical trials conducted in the United Kingdom indicate that TOLSERAM has a markedly greater activity than mephenesin, as demonstrated in the treatment of spastic and hyperkinetic conditions.

Literature gladly sent on request.

SQUIBB

E. R. SQUIBB & SONS, 17-18 OLD BOND STREET, LONDON, W.1 Tel. HYDE PARK 1733

Relief

from allergy . . .

BENADRYL, probably one of the most potent histamine antagonists, has proved to be of great value in the treatment of hay-fever, urticaria, vasomotor rhinitis, angio-neurotic oedema and, in the majority of cases, gives long looked-for relief in the skin infections and pruritic conditions associated with allergy. The Parke Davis range of products which include Benadryl provide for oral administration, topical and ophthalmic application and a solution for injection where, in acute allergic conditions, rapid action is required.

BENADRYL CAPSULES
BENADRYL ELIXIR
BENADRYL CREAM
CALADRYL
Cream and Lotion
BENADRYL OPHTHALMIC
BENYLIN EXPECTORANT
BENADRYL EMPLETS
BENADRYL PARENTERAL
BENA-FEDRIN
Nasal Decongestant

BENADRYL

A SUCCESSFUL ANTIHISTAMINE

Parke, Davis & COMPANY, LIMITED *(inc. U.S.A.)*
HOUNSLOW, MIDDLESEX
Telephone HOUNSLOW 2361

MA2178

It's a safe practice

Safety measures devised for our protection are now commonplace and readily accepted. In chemotherapy, few will deny that one of the most important of the safety measures is the careful and critical selection by the manufacturer of drugs that combine maximum therapeutic activity with minimum toxicity. Nowhere is this better seen than in the case of 'Sulphatriad'.

When sulphonamide therapy is indicated, the prescription of 'Sulphatriad' for young and old has been clinically proved and accepted as a practice with a wide safety margin and range of effectiveness. ***Detailed literature is available on request.***

PRESENTATIONS

0·5 gramme tablets and suspension. Each tablet and 3·6 c.c. (approx. 1 teaspoonful) of suspension contains 0·185 gramme sulphadiazine, 0·185 gramme sulphathiazole, and 0·13 gramme sulphamerazine — three of the most active sulphonamides.

'SULPHATRIAD'

trade mark *brand*

COMPOUND SULPHONAMIDES

for fast therapeutic effect plus greater clinical safety

AN **M&B** brand MEDICAL PRODUCT

MANUFACTURED BY

MAY & BAKER LTD

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CHEMOTHERAPY OF TUBERCULOSIS

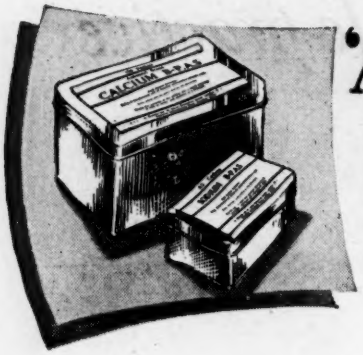
The concurrent use of PAS salts and Isoniazid is now fully recognized as a major therapeutic measure against all forms of tuberculosis.

'Aminacyl' BRAND PAS Salts

'Aminacyl' PAS products, with the exception of the Granulate (Ca PAS only), are available as either Sodium PAS B.P. or as the Calcium Salt.

They include whatever commonly used forms may be prescribed in terms of physicians' choice and patients' preference—

PACKS: *Cachets*	1.5 g.	100's	500's
	2.0 g.	80's	400's
Dragées	0.5 g (plain)	250's	1,000's
	0.75 g. (enteric-coated)	250's	1,000's
Bulk Powder		1 kg.	5kg.
Granulate (Ca PAS)		400 g.	2,000 g.



'Aminacyl' BRAND B-PAS (Calcium 4-Benzoyl PAS)

This new modification of PAS has the advantage of providing therapeutic effect comparable with that of Na and Ca PAS, but with smaller dosage. Furthermore, it is completely non-toxic, and is almost completely tasteless.

PACKS: 'Aminacyl' Ca B-PAS Powder: Tins of 150 and 500 envelopes each 3.5 g.

'Aminacyl' Ca B-PAS Cachets: Tins of 80 and 400 × 1 g.

'Aminacyl' Sodium B-PAS Cachets are also available in tins of 80 and 400 × 1.5 g.

'Pasinah' BRAND combined PAS/INAH Cachets

for convenient prescription of PAS and Isoniazid concurrently

'PASINAH' Cachets each contain 1.5 g. Na PAS (Sodium *p*-Aminosalicylate B.P.) and 17 mg. Isonicotinic Hydrazide.

PACKS: Standard Tins of 100 and 500. Details of institutional quantities on request.

Further information from the Medical Dept.

A. WANDER LIMITED

42 Upper Grosvenor St., London W.1. Phone: GROsvenor 3931.

CANADA: A. Wander Ltd., Peterborough, Ontario. AUSTRALIA: A. Wander Ltd., Devonport, Tasmania. NEW ZEALAND: A Wander Ltd., Christchurch. INDIA: Grahams Trading Co. (India) Ltd., 16 Bank Street, Bombay. PAKISTAN: Grahams Trading Co. (Pakistan) Ltd., P.O. Box 30, Karachi. CEYLON: A. Baur & Co. Ltd., Colombo.

M.387

Clearing the Channel

An action firm but gentle, prompt but lasting—that is the requirement when clearing nasal congestion. 'Vasylox', a new vasoconstrictor, meets this need. 'Vasylox' restores free breathing without causing central stimulation, sleeplessness, or interference with ciliary motility. Neither irritating nor stinging, it may be used for patients of any age, even for infants. 'Vasylox', which contains 0·25 per cent of methoxamine hydrochloride, is issued in 1/2 oz. bottles with separate dropper.

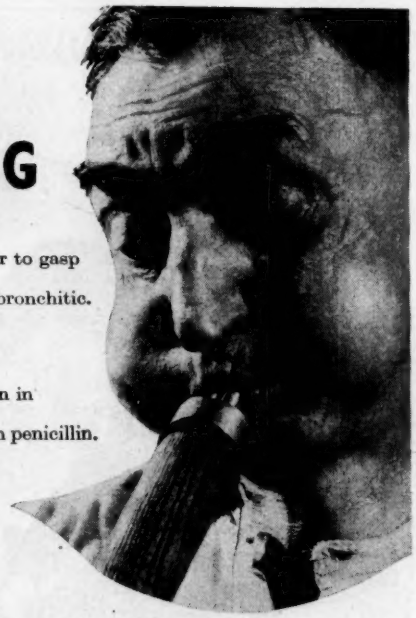
'VASYLOX' FOR NASAL CONGESTION

SOLUTION OF METHOXAMINE HYDROCHLORIDE

BURROUGHS WELLCOME & CO. (THE WELLCOME FOUNDATION LTD.) LONDON

27

BREATH TAKING



A Glass blower practising his ancient craft

It is one thing to gasp for breath for a living . . . quite another to gasp for breath to live. Yet how often this fate befalls the chronic bronchitic.

How often . . . but how seldom is it inevitable.

Estopen rapidly reduces coughing and sputum production even in those obdurate cases that fail to respond to high doses of sodium penicillin. Estopen has unique affinity for the lungs—flooding the inflamed tissues with high, sustained levels of penicillin.

ESTOPEN *Trade mark*

penethamate hydriodide

reaches the lung in strength

Single-dose vials of 500,000 and 1,000,000 units. Boxes of 10 vials

Research Laboratories : Manufacturers of medical products and foods. Agents or associate companies in almost every country in the world

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX ENGLAND

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developing problems ended with this

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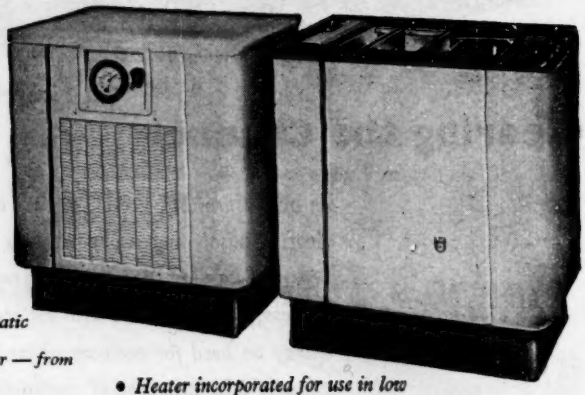

- *Thermostatically controlled — fully automatic in action.*
- *Will cool 20 galls. of water per hour — from 105°F. to 65°F.*
- *Film capacity — 60 per hour.*
- *Films always washed in cooled water.*
- *Separate Tank and Cooler. Cooler can be installed outside dark room.*
- *Heater incorporated for use in low ambient temperatures.*
- *All insulation material insect-proof.*
- *Complete and easy access for inspection.*

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Users commend its performance and reliability

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PHILIPS ELECTRICAL LIMITED

X-RAY DEPARTMENT CENTURY HOUSE SHAFTESBURY AVENUE · LONDON · W.C.2

ID962A)

HAZARDS OF BLOOD-TRANSFUSION*

J. D. JAMES
M.R.C.S.
DIRECTOR, NORTH LONDON BLOOD TRANSFUSION CENTRE

SINCE the 1939–45 war, and partly because of it, treatment by blood-transfusion has come to play a very big part in the practice of medicine. Before the war a blood-transfusion was a dramatic event worthy of press mention and not without value as a talking-point in the home circle, and this was reasonable enough because in those days a blood-transfusion effectively given might rightly be said to have saved a life that otherwise would have been lost.

Nowadays, as a result of experience gained during the war years, a National Service exists which last year distributed nearly 600,000 bottles of blood. Transfusions were given as part of the complex technique of lengthy and intricate operations, thus lessening the risk of failure; in cases of anæmia, either as an adjunct to orthodox therapy or because such treatment was not proving successful; postoperatively to assist recovery and to shorten convalescence; and in urgent cases to save a life otherwise despaired of.

Now this country-wide—in fact world-wide—extension of blood-transfusion treatment has brought its not unexpected problems along with it. Although in the past the dangers of blood-transfusion were not very apparent, partly owing to a lack of knowledge on our part and partly to mathematical reasons, it has now become a commonplace catch-phrase to say that the mortality attached to blood-transfusion is similar to that associated with uncomplicated appendicectomy. Whether this is true or not, it is intended to emphasise the fact that a blood-transfusion, like marriage, should not be lightly entered into but approached with care and competence.

It must be evident, too, that the risk attached to blood-transfusion varies in proportion to the care and skill practised by those giving the transfusion. Though this is true of most medical and surgical procedures, it is not always appreciated that blood-transfusion is well up the list of procedures deserving special attention. Too often a junior member of the hospital staff will be instructed by his chief to give a transfusion and will find himself in much the same position as the Earl of Cardigan at Balaclava, and with much the same result—only minus the glory.

The factors which give rise to these dangers can be conveniently categorised as follows:

(1) Those associated with the donor.
(2) ,, ,, ,, the stored blood.
(3) ,, ,, ,, the act of transfusion.
(4) ,, ,, ,, the recipient.

Factors Associated with Donor

Homologous Serum Jaundice

Such jaundice, produced by a transmitted virus of infective hepatitis, is now a well-known complication of transfusion with either whole blood or plasma, and subsequent fatalities are unhappily not rare. Steps to reduce the incidence of this disease are being taken, in that all would-be donors with a history of jaundice, or contact with the disease within six months, are rejected. This is by no means a fully comprehensive measure, because cases of subicteric infective hepatitis might be missed though they might still be capable of transmitting the virus. Ultraviolet irradiation of plasma did not fulfil its earlier promise, and is not now practised. Before the system of screening all donors suspected of harbouring the virus was instituted, a survey made in the Liverpool region to determine the number of cases of jaundice resulting from transfusions of plasma and of whole blood showed that jaundice ensued after transfusion in 11·9% of patients who received large-pool plasma, 1·3% of those who received small-pool plasma, and in 0·8% of those who received blood alone. The proportion of those dying as a result of jaundice was 0·2%, and at that time 0·35% of all donors appeared to be carriers of the virus. This figure is high enough to warrant the rejection of donors who are possibly carriers. Perhaps those who have been tattooed should also be rejected. No such survey has been made since screening was introduced, but no doubt it will be, because without it one cannot ascertain the facts, these cases of transmitted jaundice not being notified very strictly.

Allergic Reactions

These reactions are not in themselves of serious consequence but may, in conjunction with a critical clinical condition, be sufficient to tip the scale in the wrong direction. These reactions develop when blood containing some antigen, which we call atopen, is transfused to a person whose plasma contains the equivalent antibody or reagin. Where this condition is suspected, it is wise to test the patient before transfusion by an intravenous injection of 10 ml. of plasma; if a positive result is obtained, only washed red cells should subsequently be given.

Tropical diseases can be transmitted by transfusion, particularly malaria, relapsing fever, yaws, and kala-azar. The only method of preventing this is to reject donors who have had any of these complaints. A high proportion (about 2·7% in our region) of would-be donors have had malaria. Since most of them have undergone modern chemotherapy and many years have elapsed since the attack, the risk that parasites may still be present in the body is perhaps slight. Sometimes a donor does not know that he has had malaria and transmits it to the recipient of his blood.

Other Infections

Donors in the preclinical stage of measles and influenza have been known to transmit the virus, and recently vaccinated and inoculated donors might also effectively produce untoward results in a recipient.

Factors Associated with Stored Blood

Contamination

Danger arising from the factors involving the bottle of blood hinges mostly on the possible presence of organisms in sufficient numbers to produce clinical symptoms. The blood can become contaminated by mischance or error in the technique of collecting or by faulty autoclaving of the equipment, and the contamination may be enhanced by faulty storage, organisms which are usually discouraged from multiplying by being kept at 4°–6°C being encouraged by a higher temperature.

I have previously described (James 1953) the numerous precautions taken by the Blood Transfusion Service to ensure that the chances of introducing organisms into the blood bottle are reduced to a minimum, and happily enough the results so far appear to justify these steps.

A further inhibiting factor is the known bactericidal property of fresh blood. I am not altogether convinced that the refrigeration of blood directly it is collected and during transportation to the transfusion centre is entirely correct. The bacteriostatic and bactericidal properties of blood might act with greater advantage if the blood were kept longer at a temperature about 37°C, especially since the commonest contaminants, the coliform group, flourish at 4°C. The survival-rate of stored cells is not affected by lack of refrigeration during the first few hours after collection. Faulty storage at the transfusion centre might, however, encourage the growth of the organisms which have survived their initial entrance into the blood and normally multiply at room-temperature or

* A paper read to the Southend-on-Sea Hospital Medical Society on April 29, 1954.

37°C. Thus a careful check of the temperature of the refrigerator both at the transfusion centre and in hospital banks is very necessary.

By far the greatest trouble in the past has arisen from those organisms, such as atypical coliforms, which multiply at refrigerator temperature; hence it may be very profitable to make a stained film of the blood before giving it. Certain non-hæmolytic organisms may be present in great numbers in the red-cell layer without an appreciable visual change being apparent in the plasma layer—i.e., the absence of hæmolysis in the bottle does not preclude infection.

In the laboratory it is wise to remember that, no matter how meticulous the technique, it is dangerous to use blood which has been sampled for testing and then not used, especially if twenty-four hours has elapsed after such sampling, even if the bottle has been in the refrigerator the whole time. I appreciate the dilemma that arises between not wanting to waste blood and wanting to give the greatest possible help to the surgeons. The legal difficulties (James 1953) having been resolved, pilot bottles are being introduced in this region, which fact, I hope, will lead to the removal of at least one straw from the pathologist's back.

Free Hæmoglobin

The length of time blood may be stored is limited to three or four weeks after collection, after which time some hæmolysis takes place. Though it has been shown that the introduction of relatively small amounts of free hæmoglobin does not cause serious symptoms, it is not to be encouraged. A large amount of free hæmoglobin might affect an already embarrassed kidney.

Incompatibility

Possibly the most dramatic and most widely known risk of transfusion is due to the giving of incompatible blood to a patient. This has more usually taken place as a result of error among the ABO groups, but it has also happened where Rh-positive blood has been given to an Rh-negative patient already sensitised by a previous Rh-positive transfusion or Rh-positive pregnancy.

The reasons behind incompatible transfusions can be divided into technical and organisational. The latter has probably caused the greater number of mishaps.

I have previously explained (James 1953) the care taken at the transfusion centre to see that the bottle of blood has been correctly grouped and typed, but the possibility of error is not ignored, in that each bottle has on its label the caption "Test for compatibility before use."

Thus in the hospital laboratory lies the responsibility of seeing that, so far as the patient is concerned, a non-harmful medium is delivered to the clinician for his use. Where technical errors have been committed, it has almost invariably been due to a lapse in the very high standards necessary in this work. With so much experience gained during the last few years and the widespread publication of the best modern serological techniques it is unforgivable that less than the best should be provided. Every pathologist and technician after cross-matching a bottle of blood should ask his conscience whether he would be prepared to have it transfused into his own circulation. In some cases accidents have taken place when technicians have been interrupted while at work at the bench. When I remember that it was a rule at my hospital that the person testing a Wassermann reaction should never be spoken to, I feel that it is not too much to extend this rule to the transfusion serology, because, though it is important that the stigma and discomfort of an unnecessary course of antisyphilitic treatment should be avoided, even more so should be the chance of sudden death.

Often mismatched transfusions have been due to inexperienced members of the staff making the tests at night or at weekends in the absence of expert members. Therefore every effort must be made to ensure a 24-hour 7-day service for transfusion work, and I think this can be done providing it is not abused by the thoughtless.

As already stated, the errors arising from bad organisation may outnumber those from faulty technique, and cases have arisen where the wrong blood has been given owing to the incorrect labelling of the bottle or of a specimen of blood taken at the bedside. In one tragic case the blood responsible was intended for another patient of the same name in the same ward. No matter how outlandish the name, it is no guarantee that there is no other patient of the same name in the hospital. In Wales the problem becomes lesser or greater according to how you look at it, because the odds against a ward being inhabited by patients all named David Jones cannot be very large. To overcome this danger arising from duplicated names every possible step must be taken. The patient's full names, age, address, and hospital number should be written on the cross-match label and verified with the patient before transfusion is started.

It is most important that the label should not be attached to the bottle until *after* the cross-matching has been done and the compatibility of the blood established. Failure to do this has led to tragedy.

Not long ago a nurse was given a bottle of blood in the laboratory and told that it had been cross-matched for malæna. She took it up to the correct ward, but the blood was given to a woman named Melina; she fortunately recovered.

Most of these accidents could be prevented by a system of double checking by more than one person, with signatures given as evidence that some positive step has been taken to see that the right bottle goes to the right patient. No matter how seemingly tedious these precautions are they must be practised. In laboratories where mishaps have occurred it invariably becomes the rule that everybody immediately becomes aware of the necessity for tightening up the control of blood, and the strictest regulations to this effect are introduced, with belated enthusiasm.

Recently attention has been drawn in America to the dangers of giving large transfusions of group-O blood to patients belonging to groups other than O, this having been the practice in forward areas in Korea. The danger lies in the presence of anti-A and anti-B agglutinins and hæmolysins in the plasma of the donor blood. When several bottles of group-O blood have been given these agglutinins and hæmolysins may rise to a high proportion of the patient's circulating blood with the result that the subsequent transfusing of group-A or group-B blood could lead to disaster. In this country there has been a great improvement in this direction, and only in the tightest corner is non-homologous blood given.

Briefly the basic principles underlying the conduct of a case of transfusion reaction are as follows.

The most important lesion affects the kidneys, causing grossly diminished urinary excretion which, if not successfully treated, will lead to death from uræmia.

The kidneys suffer from anoxia owing to impairment of the blood-supply, presumably by clumps of agglutinated red cells. The original theory that the free hæmoglobin resulting from the hæmolysis of the agglutinated cells damaged the tubules is incorrect.

During this stage of functional renal impairment the aim is to give the kidney as little work as possible. So it is necessary to see that the patient is given total fluid by mouth or intravenously equal to the fluid lost through skin and lungs—about 1000 ml. daily plus the measured amount of urine passed, if any. Electrolytes lost are made up by the addition of sodium chloride and sodium bicarbonate, and calorie requirements are met with dextrose and peanut oil. When the stage of diuresis is reached, a careful watch must still be kept on the fluid and electrolyte balance. Further details of this treatment,

known as Bull's régime, are given by the Ministry of Health (1954).

This treatment is almost exactly contrary to what used to be done in these cases, when large quantities of potassium-citrate solution were given in an attempt to flush the kidneys.

Early in these cases oligæmic shock may ensue. The only proper course then is to give an immediate transfusion of compatible blood. One can appreciate the reluctance of the doctor in charge of the case to have anything further to do with blood-transfusion, but the nettle must be grasped.

Factors Associated with Transfusion

Excess of Blood

If blood is given too rapidly, especially to patients with unaltered blood volume, the venous pressure rises, and some of the added fluid will tend to remain in the blood-vessels of the lungs, with consequent risk of pulmonary œdema. Furthermore, the transfusion of excessive amounts of blood, especially in certain pathological conditions, can lead to conditions more lamentable than existed previously; again the end-result is pulmonary œdema, which may end in death in such a form that the transfusion may not be suspected as being the cause. Needless to say, if the transfusion is still in progress when signs of overloading are noticed, it should be stopped at once, and the appropriate treatment instituted.

Air Embolism

Deaths still take place from air embolism. About 10 ml. of air introduced into the circulation is sufficient to cause death, and most of the cases due to transfusion have been due to blood being given under pressure where a rapid restoration of blood volume has been thought necessary. The probable explanation is that the blood-level in the bottle is allowed to fall below the level of the outlet tube. Even if the level appears to be well above the danger mark outside the filter, it is well to remember that, if the filter is covered with clot, the level inside the filter may fall more rapidly than the level outside, and thus air can be admitted to the tubing. It is also worth remembering that air embolism can occur without the presence of positive pressure in the bottle—a blocked filter can cause it. Though the risk may be somewhat less, it is possible to introduce air into the veins by its being sucked in through loose connections or by not having the tubing filled with blood before starting the transfusion. Thus during a transfusion, especially towards the end of a bottle, the drip chamber should be carefully watched. This mishap can be prevented by being on the look-out for it and taking certain common-sense steps.

Pyrogens

Pyrogens produce a rise in temperature, and in transfusion work are understood to be the product of contamination by organism. Though the organisms may have been rendered harmless as regards infection, their biochemical remnants can produce undesirable reactions which in a seriously ill patient might be the last straw. Pyrogens are usually introduced by faulty distillation, and great care has to be taken to see that the specially designed stills are functioning properly, and that samples of the water produced are frequently tested for the presence of pyrogens. Incorrect cleaning and drying of the equipment may also be a cause, and it is well to remember that autoclaving does not produce freedom from pyrogens.

Thrombophlebitis

Within the last year or two those who have had a wide experience of transfusion therapy have been worried by the incidence of thrombophlebitis in the vein into which the transfusion or infusion is being given. Considerable investigations have been and are being made, and since this condition, which sometimes has proved quite serious, is found with substances other than blood, it has been thought that the rubber tubing was the incriminating factor.

This solution may be too facile, because, whereas the length of the transfusion bears directly on the result, and changing sets frequently during a transfusion may lessen the risk of thrombophlebitis, one also hears of hospitals where thrombophlebitis is not met with, and I have also been told that, at one large hospital, the incidence of thrombophlebitis always increases with a new influx of less experienced house-officers into the wards.

On the other hand, a certain latex rubber made in America is less often associated with thrombophlebitis. So probably the giving set is the culprit, but not the only one, if thrombophlebitis never develops when the senior pathologist gives the transfusion but only when junior members of the staff do.

Hæmolysis from Warming

Every now and again one hears of patients being transfused with blood which has been warmed with too great a zeal, thus causing rapid hæmolysis and producing extremely undesirable results. This warming of the blood before giving it is a custom taking an unconscionable time a-dying. There is no need, other than in the case of infants or of extremely cachectic patients, to warm the blood; so the nurses should be discouraged from warming it.

Excess of Citrate

At one time it was thought rather dangerous to give large quantities of sodium-citrate intravenously, but it was soon learnt that the liver largely metabolises it. Where the liver is damaged, however, the plasma-citrate level can rise considerably, and tetany has been reported in such cases. Personally I have not heard of a single case in my area, where nearly a million bottles of blood have been given, and this is probably true of the whole country; but tetany has been produced during the replacement transfusion of infants by overloading with citrate. If, however, concentrated red cells are used, the risk of this condition is practically nil.

Factors Associated with Recipient

Antibodies

From a transfusion point of view patients can be divided into two classes, normal and dangerous. The first class might give trouble; the second class, however, are much more likely to—they are the people who have had previous transfusions or have had babies. They are the people who may have in their blood-stream circulating antibodies which, on being brought into contact with the appropriate antigen in transfused blood, will produce a reaction ranging from severe discomfort to death. This means that extra care has to be taken in cross-matching to detect these antibodies which, though present in low titre, may yet cause a fatal reaction. The most sensitive test in this respect is the Coombs test; it is the only test capable of detecting the anti-Duffy antibody and the anti-Kell antibody, both of which are admittedly rare. It is considered by some that an albumin cross-match is sufficient to detect any incomplete antibody, but it should be realised that, in the case of a dangerous recipient, it is necessary to do a five-tube titration of the recipient's serum to obviate zoning. Thus in the long run the Coombs test is easier in these cases. (It is fair to say, however, that in practice cross-matching in saline solution at room-temperature, and in albumin at 37°C, should be sufficient to prevent incompatible reactions.) These tests are now so well known and tried that omission to apply them would require very exceptional circumstances to justify such a course.

Cardiac or Renal Insufficiency

In the case of a patient with cardiac or renal insufficiency there is an ever-present danger of overloading the circulation with fluid (see above), and it is very much

up to the doctor in charge to satisfy himself that these conditions are not present before adding more fluid to that already present. Where it is necessary to transfuse in these cases, it is most advisable that concentrated red cells, sometimes called packed cells, should be given. When this is done, the blood should be given within 24 hours of preparation because the manipulation required in packing the cells increases the risk of contamination.

Anæmia

In severe anæmia a circulatory adjustment takes place: venous pressure is raised and the cardiac output with it, owing to the compensating restoration of the blood volume. In this condition the heart is perhaps working at its maximal load, and any additional burden must be carefully considered. One way of dealing with this type of case (where, for example, the hæmoglobin is less than 25%) is to limit the rate of transfusion to not more than 0·5 ml. per lb. of body-weight an hour. Another way is to prop the patient up in bed, possibly to give digitalis, but above all to keep the volume transfused to less than 500 ml., preferably nearer 250 ml., and to use concentrated red cells. The patient should be watched carefully, the jugular venous pressure observed, and on the appearance of any sign of distress the transfusion must be stopped. If all goes well, another modest transfusion could be given next day.

Reagins

From time to time reactions follow transfusions when there has been no doubt that the blood given was compatible by all laboratory tests. These reactions are sometimes alarming, and in a patient whose condition is already serious they could be decisive. Some people have in their circulating plasma certain protein substances, called reagins, which can react if brought into contact with the appropriate antigen in the transfused plasma (atopen). Reports published in America give possibly an enhanced importance to this phenomenon, and suggestions have been made that it might be worth while to identify these sensitive patients by intravenous injections of 10 ml. of plasma before transfusion, so that, if they are found to be reactors, only washed cells might be given—i.e., red cells freed from plasma by first centrifuging, siphoning off the plasma, and washing the remaining cells in isotonic saline solution. I do not think that it is necessary to test each patient in this way, but certainly, where such a condition is suspected, it is most important that such a test should be made and that, if it is positive, washed cells alone should be given.

Miscellaneous

There remain the mystery cases: patients are transfused after immaculate laboratory procedures, the correct bottle is given, previous or subsequent tests for contamination are negative, the transfusion is given satisfactorily by competent staff, and yet the patient dies. These cases are puzzling because it is not always certain that all the facts are known; but there is enough evidence to leave a disquieting doubt, and, though anaphylactic reactions may be an adequate explanation for some of them, the rest remain not fully explained.

Envoi

I always feel that the nearer one's eye gets to the microscope the further away one is apt to get from the problems of the patient in the ward. This need not be so, but it does happen so very easily. That is why perhaps we are surprised that, when thousands of people every day are having introduced into their circulation a complex physiological fluid containing a vast combination of possible antigenic substances, some comprehended and some not, unexplained results are met with.

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CHRONIC CEREBRAL HYPERTENSIVE DISEASE

WILLIAM HUGHES
M.D. N.U.I., M.R.C.P., D.T.M.
AREA GERIATRICIAN

M. C. H. DODGSON
M.D. Lond.
NEUROPATHOLOGIST

DOROTHY C. MACLENNAN
M.B. Lpool
LATELY SENIOR HOUSE OFFICER
STAPLETON HOSPITAL, BRISTOL

IN 1946 Alvarez described, in middle-aged patients, personality changes associated with bizarre somatic symptoms which could be traced to "little strokes." Although he did not explicitly say so, we can infer that most of his cases were in hypertensives. The apoplectic crises of malignant hypertension have commanded the attention of many observers since Oppenheimer and Fishberg first described them in 1928.

Since then the less dramatic neurological and psychological consequences of sustained hypertension have received more attention. In this country Pickering (1948) described attacks of "transient cerebral palsy" which he attributed to thrombosis rather than to spasm of small vessels. In 2 cases in which the brain was examined after death lesions were found in the region of the basal ganglia. Some workers have reported the development of psychosis or changes in personality in long-standing hypertension (Davison and Brill 1939, Rosenberg 1940, Cantor 1952). Although many of the cases described have been in young people, the accounts of neurological and psychological changes read very much like a textbook description of "cerebral arteriosclerosis" in old age. The lesions found post mortem were concentrated in the region of the basal ganglia.

We review here 51 cases in which personality changes, emotional lability, and some degree of pseudobulbar palsy were constantly associated with chronic arterial hypertension. In 15 cases examined post mortem a constant pattern of cerebral lesions was found. Although most of the established cases occurred among old people, a sufficient number occurred in middle age, or had a history going back to the third or fourth decade, to suggest that the level of the blood-pressure rather than the chronological age was the deciding factor in the production of lesions.

Illustrative Cases

Case 1.—A well-nourished unmarried man, aged 63, was admitted to Stapleton Hospital as a senile dement on Sept. 29, 1953. His sister stated that he had been a salesman in a good position until the outbreak of war in 1939. His employment as a salesman ended then and he went to work in a factory. After a few months he became morose and unhappy, lost his job, and went to live with his sister. He was terrified of air-raids and hid himself in a wardrobe while they were on. He became careless in his appearance and cantankerous. When eating he would start with the sweet and then eat the main dish, as often as not with his fingers. He was subject to fits of rage and weeping. His gait became unsteady, and he often fell in the street and was carried home unconscious by friends. At this time there were references to high blood-pressure by the family doctor, who has since died, but records were not available. The emotional display gradually took the form of giggling. With his shuffling gait and inane laughter he became the butt of the village urchins, and his sister stated that she often wished him dead. After a fall in 1949 he was admitted to a general hospital. There he was described as emotionally facile. Questions provoked an "odd mixture of laughing and crying." There was no obvious paralysis. His blood-pressure was 250/140 mm. Hg. He was discharged after four days. A few weeks later his sister got him admitted to a hostel for old people. There his condition continued to deteriorate, until the staff would no longer tolerate his behaviour.

On admission to Stapleton Hospital he was mentally inaccessible. Any question or attempt to converse produced

explosive laughter. His blood-pressure was 160/115 mm. Hg. The ocular fundi showed "silver-wiring" of the arteries and dilated veins but no exudates.

Present State.—He is now bedfast and doubly incontinent. His hands and face are often smeared with fæces in the morning. His appetite is good, but he has to be fed. Left to himself he will eat with his fingers and is liable to fits of choking. When not disturbed his features are immobile, and he lies in bed with his head raised on a "psychical pillow," staring for long periods without blinking. His sister reports that he occasionally talks to her for a few moments rationally without giggling. His speech is slurred. At a recent visit he asked her about the health of an old friend. Then she gave him an apple, which he devoured like a wild animal and was promptly sick. She feels she does not want to see him again. His condition has remained static for the past eighteen months.

The social impacts of the disease are illustrated by this case. The next 3 cases have been selected from the 15 which came to necropsy. They show the clinical consequences of cerebral infarction in a succession of stages.

Case 2.—An unmarried casual labourer, aged 39, was admitted to hospital in June, 1953. He was rejected for military service in 1938, possibly on account of subnormal intelligence. During the four years before his admission "episodes" had occurred during which consciousness was lost. There were no previous records of his blood-pressure.

On admission after a recent stroke he had a mild left hemiparesis and was semiconscious. His blood-pressure was 210/120 mm. Hg, with pulsus alternans. His urine contained a trace of albumin, but no cells or casts. The blood-urea level was 20 mg. per 100 ml.; the blood Wassermann reaction was negative; and lumbar puncture produced clear normal fluid at a pressure of 130 mm. water. The fundi showed narrowing and "silver-wiring" of arteries on both sides, with dilated veins on the left. The right disc was œdematous, the left pale and small. There were no retinal exudates.

On recovery from coma he was apathetic, with a parkinsonian mask and a tendency to dribble. His speech was slurred, and he had difficulty in swallowing. He could answer questions, but his replies were not always accurate. He had fair orientation in time and place. He burst into tears if questions were pressed. He was doubly incontinent and very dirty in his habits.

Progress.—After making a slight recovery, during which he sat out of bed for a few days, he had a further "stroke" two months after admission. His blood-pressure fell to 150/100 mm. Hg. He developed a "wet chest" and died on Sept. 15, 1953.

At necropsy there was bilateral bronchopneumonia; the kidneys showed the characteristic vascular changes of essential hypertension: and in the brain were bilateral single infarcts involving the head of either caudate nucleus. The lesion on the right was an area of softening about 10 mm. in diameter, which also involved the internal capsule and putamen. More posteriorly a section at the level of the mamillary bodies revealed further small cavities in both putamina.

Case 3.—A man, aged 67, retired from the Army in 1938 with the rank of sergeant-major and secured a job as special policeman. He had his first stroke in 1939. His personality changed, and he became subject to emotional storms and outbursts of rage. He was frequently off duty but managed to retain his employment until 1949. In May, 1952, he had a major stroke—right hemiplegia with involvement of speech. His blood-pressure at this time was recorded by his family doctor as 230/150 mm. Hg.

On admission to Snowdon Road Hospital on June 18, 1953, he had only a slight loss of power on the right side, but ataxia was severe. He walked *à petits pas*. He had considerable dysarthria and some dysphagia. He was cheerful to the point of euphoria and subject to fits of laughter on slight provocation. His blood-pressure was 206/110 mm. Hg. The fundi showed "silver-wiring" of arteries, with dilatation and nipping of veins. There were no exudates. Urine showed a cloud of albumin. Blood-urea was 30 mg. per 100 ml.; Wassermann reaction negative.

Progress.—On July 31, 1953, he collapsed with a feeling of tightness in the chest. His blood-pressure was 200/120 mm. Hg. He recovered in a week. On Aug. 7, 1953, he developed retention of urine due to an enlarged prostate. An indwelling catheter was inserted because he was considered unfit for surgery. His physical and mental condition had by this time seriously deteriorated. He had become bedfast and incontinent, and pseudobulbar palsy was severe. Any attempt to speak ended in a grunt or a roar, and swallowing became increasingly difficult. From this point he went downhill rapidly with urinary sepsis, and he died on Nov. 7, 1953. Although he could not communicate by speech or writing he retained some insight up to the last and expressed his desires and replies to questions by awkward gestures. He was subject to fits of laughter and rage up to the last few days.

At necropsy the important findings were widespread bilatera bronchopneumonia, which was probably the immediate cause of death; benign hypertrophy of the prostate, with chronic cystitis; atheroma of the aorta and coronary and cerebral arteries; and old healed myocardial infarct. When the brain was sectioned coronally, old multiple infarcts were seen in the periventricular white matter and in the basal ganglia. On the left side a cavity about 20 mm. in diameter involved the head of the caudate nucleus, putamen, and internal capsule and communicated with the lateral ventricle. At a more posterior level the left thalamus and both putamina showed numerous small areas of softening.

Case 4.—A retired petty-officer, aged 74, had retired at the age of 50 after a successful career in the Royal Navy. About two years after retirement he developed personality changes. He became mean, suspicious, quarrelsome, and careless in his habits and was subject to fits of rage and weeping. He had frequent falls, with sometimes loss of consciousness. He lost his job as caretaker of a club, and his wife had to take on work as a "daily woman." Since she could no longer leave him alone in the house, owing to his carelessness with fires, she got him admitted to a hostel for old people in 1951. His behaviour and habits were so bad that after a week he was certified and removed to a mental hospital. His blood-pressure was recorded as 190/100 mm. Hg at this time. After six months he was transferred to Stapleton Hospital. During his stay he was bedfast, incontinent, dirty in his habits, and mentally inaccessible. He had passed into a state of dementia with muscular rigidity in which it was difficult to carry out any physical examination, including examination of the diastolic blood-pressure. After many attempts we got a reading of 140/80 mm. Hg on one occasion. There was no emotional response to questions. He lapsed into coma on Oct. 20, 1953, and died two days later.

At necropsy a large area of softening was found involving the anterior end of the caudate nucleus and the antero-superior part of the internal capsule. At the level of the mamillary bodies, which were much shrunken, the right putamen and both thalami showed very small cavities (*état vermoulu*).

Hypertension

The systolic pressure ranged from 140 to 298 mm. Hg and was higher than 160 mm. Hg in 49 cases. The diastolic pressure ranged from 96 to 160 mm. Hg and was 100 mm. Hg or higher in all but 1 case. These figures are based on the highest recorded diastolic pressure in every case. The diastolic and systolic levels fluctuated from day to day, from hour to hour, and from one minute to the next. In one case in final dementia the diastolic pressure never rose beyond 80 mm. Hg during nine months in hospital. We knew, however, from previous records that it had reached 190/110 mm. Hg before admission. The records were from his family doctor and from the Medical Officer of a mental hospital.

The duration of hypertension was difficult to estimate. The longest duration of which we have records is eighteen years. This is from a patient treated in another hospital in 1935. His blood-pressure at that time was 186/110 mm. Hg. His symptoms—weakness of the legs and dysarthria—dated back a further two years, making twenty years' duration of symptoms. It would not be unreasonable to suppose the duration of the hypertension in this case to be at least twenty years.

We could not correlate the height of the blood-pressure with the severity of the symptoms. A fall in blood-pressure after an "acute episode" was observed in

many instances. Such a fall does not always signify coronary thrombosis. As Alvarez (1946) observed in his series, it often follows strokes in hypertensives. Although we observed fluctuations in blood-pressure and severity of symptoms in such cases we could not correlate the two findings. The same tendency of symptoms to improve after an acute episode was observed whether the blood-pressure rose or fell.

Evidence of renal disease was no more frequently obtained than might be expected in patients of this age-group and was in most instances due to pyelonephritis and prostatic enlargement.

Emotional Lability

Emotional lability was a striking feature in most cases. It was the symptom which attracted our attention and led to an estimation of blood-pressure and thence to diagnosis in some of the cases in the peripheral hospitals. The range of emotional lability was very wide. Thus 2 men were virtually unapproachable; a few insignificant words or phrases reduced one of them to helpless giggling and the other to tears. Three of the male "weepers" and 1 female showed salivation or drooling similar to that noted in postencephalitics but not so severe. All 4 had well-marked symptoms of pseudobulbar palsy.

The emotional display, whichever form it took, was always explosive. It resembled the crying of infants in its sudden onset and equally abrupt termination. In 15 men and 13 women the emotional display consisted invariably in weeping, whereas in 7 men and 6 women it consistently took the form of either giggling or laughing. In some cases it was not easy to classify the initial phase of the outburst as weeping or laughing. A facetious remark calculated to provoke a smile or chuckle in a normal person might indeed induce a momentary smile. Within a second or two, however, the eyes glistened and filled, the face reddened, and the features passed into emotional spasm with loud wailing and copious weeping. In some cases the emotional display was difficult to provoke. Generally a question about home or family life proved the most effective stimulus. Like other symptoms emotional lability fluctuated in intensity.

Emotional lability was usually associated with intellectual degeneration. Although extreme lability was often associated with gross intellectual deterioration, the two processes did not run parallel in every case.

Case 5.—A man, aged 67, is known to have had a blood-pressure of 220/140 mm. Hg for four years. He is ambulant, with *marche à petits pas*, but usually sits in a chair all day. Incontinence of urine gives him a strong ammoniacal odour. Reference to this incontinence causes no obvious embarrassment. His speech is explosive, with moderate dysarthria and some dribbling. When answering questions he will break into wheezy laughter with raising of the eyebrows and lid retraction. Such spasms last only a few seconds, and often they have no relation to the context of the conversation. His answers to questions are rational, and his orientation in time and place is good. An electro-encephalogram yielded normal findings. Crude tests indicate only moderate deterioration of intellect.

Case 6.—A man, aged 54, is known to have had a blood-pressure of 200/120 mm. Hg for two years. His emotional lability is extreme. Any attempt at conversation during the past two years provoked loud and explosive wailing. An electro-encephalogram was grossly abnormal, the alpha rhythm being almost completely absent. Recently an intelligent and sympathetic male night-nurse reports that he can engage the patient in a rational conversation about 2 A.M. every morning. To avoid emotional outbursts the nurse has to be very careful about his own contribution to the discourse. During the day the patient remains highly emotional and mentally inaccessible.

Outbursts of rage occurred with the weeping or laughter in some cases, and these were more frequent in cases with aphasia or with well-marked pseudobulbar palsy. These rage reactions often created awkward situations at home and in hospital. In one instance the police were called in to settle a disturbance in the home created by an elderly male. Another man, aged 83, who could only shuffle about the ward with the aid of two sticks, was impatient with the staff who could do so little to restore his youthful vigour. The most sympathetic inquiry about his condition would end by provoking a storm of vituperation and abuse.

Pseudobulbar Palsy

One of the commonest symptoms is a difficulty in phonation which might be described as "ataxic aphonia." The patient appears to have difficulty in utilising the expiration for voice production. When he tries to speak he may have to make several attempts before any word is uttered. Often the sentence begins in a whisper, booms into a roar, and then, as the expiratory effort becomes exhausted, trails off into a wheeze. Concomitant heart-failure with dyspnœa may combine with pseudobulbar palsy to produce this characteristic effect, which corresponds closely to the conventional portrayal of the irascible apoplectic on the verge of a stroke. We have been able to demonstrate this effect in some of the earliest cases.

Signs of advanced pseudobulbar palsy were noted in 5 men and 3 women. The dysarthria in these 8 cases was so severe as to render speech almost, if not quite, unintelligible. All these patients had occasional fits of choking at meals. Pseudobulbar palsy was the indirect cause of death in one instance; the victim choked while eating and died, death being due to asphyxiation.

In many of the severe cases the patients had to be fed, and some of them would hold the food in the mouth, without swallowing, for hours at a stretch. Two women became emaciated towards the end, and in one of them at necropsy the stomach was small and empty and the intestines were collapsed. There is no doubt that inanition from dysphagia contributes to early death in these severe cases. In one instance widespread pulmonary consolidation was found post mortem in spite of liberal treatment with antibiotics and sulphonamides before death. The possibility of inhalational pneumonia could not be ruled out in this case (case 3).

Emotional lability was always noted in severe cases, but intellectual deterioration did not run parallel with the severity of the pseudobulbar palsy. Thus, 2 patients who could no longer express themselves in speech maintained prolific correspondence with their relations and could answer questions rationally and communicate their requests by writing.

Other Neurological Signs

Apart from the development of pseudobulbar palsy already described, a multiplicity of signs pointing to pyramidal and extrapyramidal lesions was observed. The neurology of cerebral arteriosclerosis has been well described by Critchley (1931), and there is little to add to this account.

Perhaps the most incapacitating symptom in the early stages was vertigo. This tendency to fall, which is a distressing feature of old age (Sheldon 1948), was exaggerated in our cases. In many ambulants the characteristic gait—*marche à petits pas*—was noted. It was interesting also to observe the tendency of those in bed to carry the head on a "psychical pillow." A very distinctive facies, characterised by immobile features, unblinking stare and some lid retraction was noted in about a third of the cases.

Personality Changes and Intellectual Deterioration

There was evidence of intellectual deterioration in every case, but the range was wide. At one extreme

was the demented patient, apathetic, incontinent, and mentally inaccessible. At the other, the degree of deterioration had to be computed by considering the previous occupation and social background of the patient, supplemented by a history of personality changes from friends or relations. These changes in personality and peculiar behavioural traits attracted more and more attention as our study progressed. An example of early intellectual deterioration is provided by the following case :

Case 7.—A female teacher, a university graduate, aged 50, with a blood-pressure of 240/130 mm. Hg and mild hemiparesis from a recent stroke, has a small income of about £3 per week. Although she made an excellent physical recovery she would sit in a chair all day and stare ahead without manifesting any interest in her neighbours. Asked why she did not look for another job she said that the net result of income-tax would be to lower her income below her present figure. Twelve years previously this woman had thrown up a safe teaching job to join a female branch of the fighting services. She had once taught mathematics in a secondary school.

A characteristic behavioural change is that which might be described as social indifference. The patient is out of sympathy with his environment. He is careless of the impact which his own behaviour produces on his family or business associates. In many cases the patient's expression and behaviour are further conditioned by the disabilities of pseudobulbar palsy. Graphic descriptions have been published of old people in the long-stay wards of institutions wolfing their food like wild animals. We have no doubt that such highly coloured pictures are based on superficial observations of this type of case.

The stage of "faulty habits" is normally associated with severe intellectual deterioration. There is the ambulant male who is careless about emptying his bladder into the urinal and adjusting his trouser buttons afterwards. The other patients complain about the ammoniacal odour and indecent exposure. The bedfast dement will pick up her fæces from the bed and offer them to the nurse, the doctor, or a visitor. Two females were coprophagous. Both had a severe degree of emotional lability—weeping—and yet in both some insight was preserved. Wilson (1940) has noted that insight is preserved longer in dementia due to cerebrovascular disease than in dementia due to other causes.

Incontinence of fæces and urine is "normal" during the unconscious phase of stroke, and nurses and relations regard it as pardonable for a brief period in convalescence. Urinary retention and sepsis tend to prolong the condition in some cases. In many cases where insight in other respects seemed to be well preserved lapses of behaviour in this respect provoked antipathy, not to say hatred, among the patient's relations, who felt that the patient could, if he wished, control his dirty habits.

Case 8.—A widower, aged 68, with a blood-pressure of 240/110 mm. Hg, living with his son and daughter-in-law, was seen at his home in consultation with the family doctor. The patient was up and about. He could dress, eat, and go to the toilet by himself. He had a stroke a year ago which left no residual paralysis. He was subject to attacks of giddiness, and since he had fallen once or twice he no longer went out. He answered questions accurately and gave no emotional display when asked about his deceased wife, his family, or his occupation. His speech was characterised by the ataxic aphonia we have described. An interview with the daughter-in-law revealed that his behaviour was normal during the day, but at night he would defæcate on the bedroom floor or lose some fæces on the bathroom floor or in odd corners. He would excuse himself on the plea of diarrhœa, but the scybala were well formed. Two nights before our visit he had urinated in a bowl of flowers, which overflowed on the table. After admission to hospital he became more emotional, and any reference to his son—but not to his daughter-in-law—would provoke a storm of weeping. Reference to his incontinence, however, provoked no emotional response.

A variant of the personality change after stroke was observed in a married woman, aged 46, whose blood-pressure was 200/120 mm. Hg. After making a good recovery from a right hemiplegia she was discharged from hospital but continued to come for physiotherapy as an outpatient. She is hyperemotional and pesters the ambulance drivers with sexual overtures. She writes passionate love letters to a male member of the staff on odd pieces of paper. These notes are written in pencil and sealed in lipstick with the impression of the lips. Before her stroke she led the life of a respectable suburban housewife.

Faulty habits had the quality of a compulsion in those cases where insight in other aspects of behaviour was well preserved. It is impossible to exaggerate the impact of these personality changes on the patients' relations and friends. In many instances it was these changes which accounted for the patients' admission to hospital and for the refusal of the relations to have them home again.

As Alvarez notes, the patient himself rarely recognises the changes in his own personality. For an objective account of the quality and magnitude of these changes it is imperative to get a history from friends or relations.

Strokes

There was a great variation in the type of stroke observed or recorded. There was the major ictus associated with unconsciousness followed by paralysis. There was the mild stroke described by Alvarez (1946, 1948) and Pickering (1950) in which consciousness was not lost but was followed by aphasia, mental clouding, or palsy. There was the "bad turn," "giddy bout," the attack of indigestion with vomiting, the sudden alteration of behaviour—all of which in the context of the case could be construed as evidence of recurring strokes.

The tendency to recover was considerable, even in severe cases. Recovery took place in the absence of special treatment and was so extensive in many cases that we were at first inclined to doubt the original account of the stroke. We observed instances of phenomenal recovery in a few cases while they were under observation in the wards. Usually the strokes were little and often, and the ensuing recoveries almost but never quite complete.

Ophthalmological Changes

The fundi were examined in every case where such examination was practicable—a total of 36 cases. The difficulties in the way of detailed examination of a group of such cases will be obvious. The intelligent coöperation of the patient was rarely obtained, and some of the dements resisted all attempts to examine them. Our results, which in the circumstances must be regarded as preliminary, show that some degree of "arteriosclerotic" change was observed in all the cases examined. Our experience is not sufficient to say how far this is a departure from what is normal for the age-group. The common changes observed were narrowing, tortuosity, and "silver-wiring" of the arteries. In 4 cases occlusion of a terminal branch was observed. The veins were dilated in comparison and nipped at the crossings. Exudative lesions, which included "cotton-wool" patches and flame-shaped hæmorrhages, were seen in 6 cases. In 4 of these there was sufficient œdema of the disc to fit them into group IV of Keith, Wagener, and Barker's (1939) classification of hypertensives.

At this stage of our investigation we believe that the absence or infrequency of exudative lesions may prove an important point in the differentiation of the syndrome from malignant hypertension. We note, however, that in any large group of published cases of malignant hypertension there are a few cases similar to our own.

At the same time, a few of our cases might be classified on ophthalmological findings as malignant hypertension.

Pathology

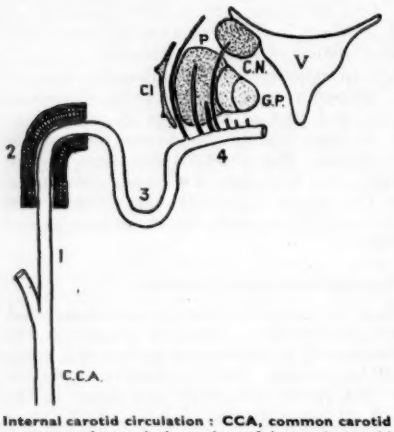
In each of 15 cases coming to necropsy there were multiple small lesions in the brain, representing different stages in the organisation of areas of ischæmic softening. The heads of the caudate nuclei were constantly damaged; in some cases the lesions were virtually confined to these nuclei and to the anterior parts of the putamina. On the other hand, the inner segment of the globus pallidus was spared in every case. About two-thirds showed small scattered lesions in the thalamus, whereas midbrain, pons, cerebellum, and medulla oblongata were each involved on one or two occasions only.

Macroscopic infarction of the cerebral cortex was seen on two occasions only, but in both instances by far the greater part of the cortex remained unaffected. Histological evidence of nerve-cell loss was not obtained in the small number of sections examined.

Histological examination of cerebral arteries of all sizes showed various degrees of arteriosclerosis but no persisting evidence of total occlusion, although the brain lesions were clearly ischæmic.

Discussion

We have had some difficulty in accounting for the presence of ischæmic lesions in these brains. Hicks and Warren (1951) had previously been unable to demonstrate vascular occlusion in 100 cases of recent cerebrovascular accident, and others have had the same experience. It has been suggested that lesions such as these may be the result of arterial spasm. Although spasm may be an important factor in their production, this is impossible to demonstrate or to verify with certainty. Moreover, the cerebral cortex, with its more copious blood-supply, might be expected to undergo relatively greater damage from vasospasm than the rest of the central nervous system. In fact, the reverse is the case.



Internal carotid circulation: CCA, common carotid artery; 1, cervical portion of internal carotid artery; 2, intra-osseous portion; 3, intracranial loop; 4, origin of perforating arteries from anterior and middle cerebral arteries; Cl, claustrum; P, putamen; GP, globus pallidus; CN, caudate nucleus; V, ventricle.

Lesions occur mainly in the territories supplied by the perforating arteries. The selection of these vessels can perhaps be explained in terms of hydrodynamics. The effect of narrowing a tube through which a fluid is passing is to increase the speed of flow on the distal side of the constriction. At the same time, hitherto streamline flow tends to become turbulent, with the formation of eddies, as a result of which the head of pressure falls. The internal carotid artery (see accompanying figure) is constricted, or its expansion is curtailed, as it passes through the carotid canal. Within the skull it forms a loop in the lax extradural tissues before giving off its terminal branches. In normal circumstances turbulence might be expected in the proximal part of the loop, but by the time the perforating arteries are reached flow is probably once more streamline. In the presence of arterial hypertension, alone or combined with arteriosclerosis, eddies might develop as far distally as the mouths of the perforating arteries, reducing the flow of blood within them sufficiently to cause ischæmic lesions in parts of the central nervous system which they supply.

Essential hypertension is common and cerebral arteriosclerosis is an almost physiological accompaniment of advancing years. Fortunately, serious cerebral damage is a rare complication. Why some people succumb in this way and others do not remains unsolved. Possibly liability to cerebral damage, in the presence of other predisposing factors, may depend on individual features of the anatomy of the cerebral blood-supply. The testing of this hypothesis would require a method for the investigation of blood-flow in selected territories of the brain.

The existence of a group of cases such as we have described has not hitherto been recognised, although scattered accounts of individual cases of cerebral arteriosclerosis and malignant hypertension have been published. The limits of this group are defined by finding hypertension in every case, by the development of emotional lability and pseudobulbar palsy, by personality changes, and by the tendency to end in dementia. From our study of the pathology so far it appears that all these profound changes in behaviour and personality derive from lesions in the basal ganglia while the cerebral cortex remains intact.

Summary

A study of 51 hypertensives showing clinical evidence of cerebral damage is reported. The incidence in the sexes was about equal. Most of the patients were elderly, but a few were middle-aged.

The clinical pattern was characterised by frequent small strokes with transient or permanent paralysis and a tendency to develop pseudobulbar palsy in the course of time.

Characteristic personality changes included emotional lability and intellectual deterioration.

The disease is chronic, with an observed duration of $1^1/_2$–20 years. It tends to start somewhat earlier and to run a more rapid course in males than in females. Those who survive long tend to drift into dementia.

At necropsy on 15 cases there were multiple foci of softening involving subcortical centres, including the striatum (caudate nucleus and putamen) in every case and the thalamus in 11. These lesions were predominantly in the territory of the perforating arteries. A tentative explanation of their distribution in terms of hæmodynamics is put forward.

We wish to thank the many doctors and nurses in and out of hospitals in the Bristol Clinical Area who coöperated with us in this investigation, in particular the pathologists, Dr. N. J. Brown and Dr. H. Urich of the Southmead Group of Hospitals and Dr. A. T. F. Rowley of the Weston-super-Mare Group, who have allowed us to use their necropsy material and records, and to Dr. W. Grey-Walter, director, Electrophysiological Department, Burden Institute, for electroencephalographic investigations in cases 5 and 6.

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CLINICAL INVESTIGATION OF ALLEGED ANTAGONISM OF CORTICOIDS

ROY GOULDING
B.Sc., M.B. Lond.
LECTURER IN PHARMACOLOGY, MEDICAL SCHOOL

K. S. MACLEAN
M.A., M.D. Camb., F.R.C.P.
ASSISTANT PHYSICIAN AND ASSISTANT DIRECTOR, DEPARTMENT OF MEDICINE

J. M. ROBSON
D.Sc., M.D. Leeds, F.R.S.E.
PROFESSOR OF PHARMACOLOGY IN THE UNIVERSITY OF LONDON AT THE MEDICAL SCHOOL

GUY'S HOSPITAL, LONDON

ACCORDING to Selye (1950) numerous experiments suggest that "mineralo-corticoids and gluco-corticoids mutually antagonise each other." He defined mineralo-corticoids as those corticoids which are particularly effective in causing retention of salt and loss of potassium (e.g., deoxycortone) and glucocorticoids as those particularly effective in raising the liver-glycogen and blood-sugar levels (e.g., cortisone).

Bauer et al. (1951) point out that this is a modification of Selye's original thesis, in which he had suggested that rheumatoid arthritis was due to excessive production of the salt hormone, and had then implied that, in so far as reactions to stress were mediated through the pituitary gland, the production of adrenocorticotrophic hormone must have been simultaneously enhanced. When Hench et al. (1949) showed that corticotrophin could produce dramatic improvement rather than deterioration in rheumatoid arthritis, Selye reinterpreted his earlier findings. He stated as a general principle that "in many respects, the two types of corticoid hormones antagonise one another" (Selye 1951). He was firmly of the opinion, moreover, that "an unfavourable gluco-corticoid/mineralo-corticoid balance" was an ætiological factor in the rheumatic diseases.

Much of the evidence on which this idea is based has been derived from experiments on animals. Thus, under the influence of deoxycortone, adrenalectomised rats develop "arthritis" much more easily than do intact controls, presumably owing to the presence in the latter of some adrenal principle antagonising the arthritic-producing effect of deoxycortone. Again, the "arthritis" induced in rats by the injection of either formaldehyde or a 10% suspension of mustard into the region of the joints is aggravated by pre-treatment of the rats with deoxycortone, and inhibited by cortisone and corticotrophin. Furthermore, the permeability of the synovial membranes in rabbits, measured by the speed of absorption of phenolsulphonphthalein from the joints, is much increased by deoxycortone but diminished by cortisone. Yet, as Bauer et al. (1951) again pertinently observe, the experimental "arthritis" so studied is not necessarily related to the clinical rheumatoid condition; and hence, so far as man is concerned, such conclusions regarding antagonism of steroids are no more than deductive reasoning.

Selye himself evidently considers that this part of his theory calls for special defending. He admits (Selye 1951) that the claim that deoxycortone does not aggravate rheumatoid arthritis constitutes "one of the most justified objections raised against the Adaptation Disease concept." Though Bauer and his associates state that deoxycortone in larger doses had no such effect on their patients with rheumatoid arthritis, despite considerable retention of salt, they lay themselves open to Selye's counter that "none of the latter cases has been reported in detail . . ."

It was to test this alleged antagonism of corticoids in man that the present experiments were devised.

Methods

Patients with acute rheumatoid arthritis, thought suitable for this investigation, were admitted to hospital. A case-history was taken and a full clinical examination made. Although no elaborate or specialised tests were used to record the state of the joints, the amount of swelling, movement, and pain was carefully observed by coöperating physiotherapists who, throughout the course of each patient's stay in hospital, were unaware of the specific treatment. Preliminary investigations included full blood picture, including eosinophil chamber-count; erythrocyte-sedimentation rate (E.S.R.) (Westergren); serum-sodium and serum-potassium levels; radiography of the chest; electrocardiography; body-weight; and blood-pressure.

During their stay in hospital the patients were given a normal diet according to appetite. The only treatment, apart from the corticoids prescribed, was daily physiotherapy. The patients were encouraged to be up and about, so far as their general condition permitted.

Specific treatment extended over four stages:

(1) A preliminary period of about a week for observation and standardisation, when the only injections were 1 ml. of intramuscular sterile saline solution daily.

(2) Intramuscular cortisone (in addition to intramuscular saline solution) 100 mg. daily until a satisfactory, though not necessarily complete, remission of the rheumatoid arthritis was achieved. Thereafter the dose was reduced until the minimum required to maintain the patient without further relapse was attained.

(3) Continuation of the cortisone at the minimal maintenance dose, along with intramuscular deoxycortone acetate 20 mg. daily * instead of the saline solution. This lasted at least seven days.

(4) A concluding phase in which cortisone alone was given at the previous maintenance dosage.

Regular observations throughout the trial included periodic clinical assessment, including regular examination of the joints and recording by the physiotherapist; daily fluid chart; daily weighing, wherever practicable; daily blood-pressure readings; frequent estimations of the E.S.R. (Westergren); weekly eosinophil chamber-counts; and weekly estimations of plasma-sodium and plasma-potassium levels.

Illustrative Case-report

Case 4 (see table).—A housewife, aged 62, had suffered increasing stiffness and pain in all joints for six years. Before this she had been very active. When rheumatoid arthritis was first diagnosed, and only her hands were affected, she was given gold injections, from which she derived complete relief. Eighteen months later, however, the arthritis recurred and became more widespread. A second course of gold injections was of little avail. Thereafter her condition deteriorated and she was unable to work.

On admission, the joints affected were the neck, shoulders, elbows, wrists, hands, knees, and ankles. Pain was severe, and there was evidence of considerable loss of weight.

Treatment and Progress.—For the seven days during which the patient was given intramuscular saline solution daily there was no alteration in her subjective state or in the objective records; but over the next twenty-two days, on which she received cortisone 100 mg. daily, she showed a striking improvement. Her pulse-rate fell from 90/100 to 70/80, body-weight increased from 105 to 108 lb., and plasma-sodium level rose from the original and somewhat depressed figure of 312 mg. to 340–345 mg. per 100 ml., but the plasma-potassium level (16·3–18 mg. per 100 ml.) was unchanged. The fluid balance was unaltered. Impressively, though, the E.S.R. fell from 40 to 8 mm. in the first hour, and the eosinophil chamber-count from 80 to 15 per c.mm. Clinically the patient was far better, but her knees, in particular, remained stiff and painful. Since it was felt that, at this

* In case 1 alone the dose of deoxycortone was 10 mg. daily to begin with and 20 mg. daily subsequently.

juncture, no further advance might be possible, the cortisone was continued, but deoxycortone was given along with it at the rate of 20 mg. a day. Over the ten days of this combined therapy there was no sustained alteration in the patient's condition, either generally or in the individual joints. Her weight continued to increase, her plasma-sodium level dropped to 320–330 mg. per 100 ml., and a single eosinophil chamber-count during this period showed a figure raised to 120 per c.mm. By contrast, the E.S.R. remained less than 12 mm. in the first hour. During the last eight days that she remained in hospital, receiving only cortisone 100 mg. daily, the patient made very slight further improvement clinically; the E.S.R. remained 13 mm. in the first hour or less; the plasma-sodium level again rose to 338 mg. per 100 ml.; and a single eosinophil chamber-count again gave a reduced figure of 30 per c.mm.

Discussion

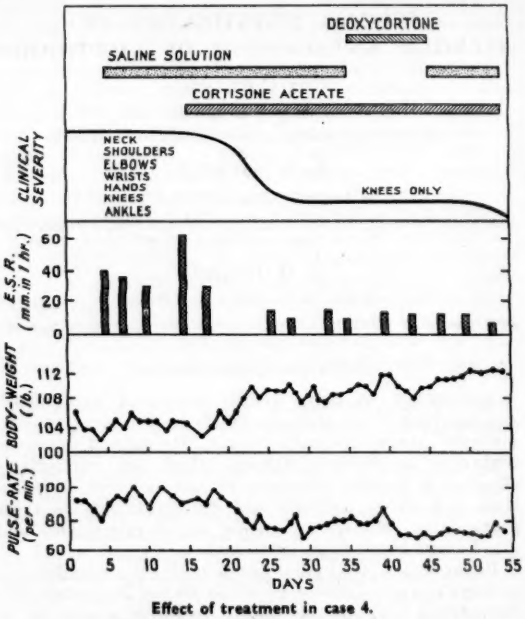
Before any conclusions are drawn from the results of the present experiment, two points arising from its design must first of all be settled: the significance of the doses used, and the availability to the body of the drugs administered.

Dosage

The doses of cortisone were moderate but, by the very *criteria according to which they were adjusted, no more* than the bare minima required to afford the patient relief in each case.

The dosage of deoxycortone probably raises a much more controversial issue. Selye (1951) contends that "in most cases, patients with rheumatoid arthritis have been treated with very small doses of D.O.C.A." Elsewhere *(Selye 1950), however, he states that "about 10 mg. of* D.O.C.A. a day, over a period of weeks, would be pathogenic in man." In the present experiment the deoxycortone was admittedly not exhibited for "a period of weeks." Nevertheless as much as 20 mg. a day was given for as long as two weeks in some instances.

There is not much information on the response of a *healthy adult to doses of this order,* but R. I. S. Bayliss (personal communication) states that in normal subjects



Effect of treatment in case 4.

it was difficult to induce either œdema or hypertension by giving deoxycortone; in one case he gave as much *as 80 mg. a day without adverse consequences.* By contrast, in the treatment of Addison's disease as little as 5 mg. a day can produce an effect.

Availability to the Body

Selye (1951) has drawn attention to the possibility that "in the few patients who received toxic amounts

SUMMARY OF CASE-HISTORIES

Case no.	Sex	Age (yr.)	Duration of disease (yr.)	Joints affected	Severity	*Response to treatment*								
						Cortisone alone (first period)		*Cortisone + deoxycortone*				*Cortisone alone (final period)*		
						Daily maintenance dosage (mg.)	Clinical condition at end of first period	Daily dosage		Duration (days)	Clinical progress	Daily dosage (mg.)	Duration (days)	Clinical progress
								Cortisone (mg.)	Deoxycortone (mg.)					
1	F	51	1	S, W, H, B, K	Moderate	50	Symptom-free	50 50	10 20	6 7	Very slight deterioration	50	5	Deterioration persisted
2	M	49	1½	N, S, W, F, K	Moderate	80	Slight stiffness in hands and shoulders	80	20	9	Slight deterioration	80	21	*Possible slight* improvement subjective only
3	F	30	2	N, S, E, W, F, K, A, T	Advanced	80	Pain and stiffness in wrist and knee	80	20	7	No change	80	10	Slight further improvement
4	F	62	6	N, S, E, W, H, K, A	Fair	100	Knees stiff and painful	100	20	10	No change	100	8	Very slight further improvement
5	F	54	3	N, E, W, F, K, A, T	Extreme	100	Generalised stiffness	100	20	10	Improvement	100	12	Improvement maintained
6	M	70	1½	N, E, W, F, K, A	Moderate	50	Stiffness and swelling *of one knee only*	50	20	13	No change (but some rise in E.S.R.)	50	6	Condition unchanged (including E.S.R.)
7	F	23	1	E, W, F, K, A	Advanced	50	Generalised stiffness and limited movement	50	20	13	Improvement	50	8	Continued improvement
8	F	58	½	W, F, K	Moderate	75	Symptom-free	75	20	11	No change	75	8	No change

A, ankles. B, back. E, elbows. F, fingers. H, hands. K, knees. N, neck. S, shoulders T, toes. W, wrists.

the *availability* of the mineralocorticoids may not have been the limiting factor." That both the cortisone and the deoxycortone should have gained access to the body generally should have been assured, in the present experiment, by their being given as intramuscular injections.

It was hoped that, by studying the urinary excretion of corticosteroids chromatographically in selected people, evidence would be obtained to show that both drugs were also being metabolised in the body. Unfortunately the results so derived were by no means consistent. To attempt any conclusions in these circumstances would therefore be valueless. We are nevertheless very much indebted to Prof. C. H. Gray and Miss Barbara Lunnon, of the department of chemical pathology, King's College Hospital Medical School, for the extensive work they undertook in this connection.

The relative dominance and interaction of the two corticoids was not reflected in, say, the fluid balance or, more particularly, the plasma-sodium and plasma-potassium levels; and the eosinophil estimations are hardly reliable as a critical measure.

Clinical Responses

From the clinical progress of these eight patients during the experiment it will be apparent that, by the end of the first stage on cortisone alone, not all were completely cured, but at least they were in the greatest possible state of remission, fluctuating a little day by day but neither progressing nor regressing over-all.

Then, when deoxycortone was given as well as cortisone, no dramatic change was observed in the condition of any of the patients. In two there was very slight deterioration, in another two further improvement, and in the remaining four no alteration at all. There was not convincing evidence of antagonism between corticoids, at least with the dosage used.

Subsequently, when the deoxycortone was withdrawn and the cortisone was once again continued alone, of the two patients who had regressed slightly one continued to regress, whereas the other recovered a little; the two that had improved continued to do so; and of the four that had been unchanged two remained thus and two improved further slightly.

Conclusions

Once the maximal improvement had been achieved, further fluctuations seen during the period of combined treatment with deoxycortone and cortisone and in the final week of cortisone administration were insignificant and probably accounted for by the natural waxing and waning of the rheumatoid arthritis.

From this small clinical trial it therefore appears that the administration of deoxycortone exerted no adverse effect upon the protective action of cortisone.

If rheumatoid arthritis is the outcome of mineralocorticoid-glucocorticoid imbalance, the effective disproportion must be a good deal greater than that attained as a result of administering the fairly large doses of deoxycortone used in the present experiment. Possibly cortisone and deoxycortone are the wrong examples to choose of the two groups of adrenocorticoids. The aldosterone of Simpson et al. (1952) was suggested as a more suitable mineralocorticoid to select than the deoxycortone used in this instance. On the other hand, there is evidence that aldosterone, possessed as it certainly is of mineralocorticoid properties, has cortisone-like features as well (*British Medical Journal* 1954). This being so, aldosterone appears unlikely to offer any more effective opposition to cortisone when used on patients with rheumatoid arthritis.

Summary

To test clinically the contention that mineralocorticoids and glucocorticoids antagonise each other eight patients with active rheumatoid arthritis were studied.

For each patient the minimal maintenance dose of cortisone was determined that would give the most relief from the rheumatoid arthritis.

While this dose of cortisone was being administered deoxycortone was given as well, at the rate of 20 mg. a day for one or two weeks.

During this phase of combined therapy no patient showed any significant change, either subjectively or in the objective condition of the joints.

Estimations were made, at the same time, of body-weight, fluid-balance, plasma-sodium and plasma-potassium levels, blood-pressure, E.S.R., and blood eosinophils. Only the E.S.R. figures were informative.

It was concluded that, in patients with rheumatoid arthritis, no mineralocorticoid-glucocorticoid antagonism can be demonstrated when deoxycortone and cortisone are chosen as examples of these two groups, and these drugs are used in the usual therapeutic doses.

We thank the Medical Research Council for generously supplying the cortisone used in this experiment; the ward sisters and nurses, who went to so much trouble in their coöperation and in the care of the patients; the physiotherapists, who not only contributed so much to the well-being of the patients but also undertook the arduous and responsible duty of examining and recording the condition of the joints regularly; and all those who made the ancillary investigations.

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CONTINUOUS GAS ANALYSIS IN THE CONTROL OF OXYGEN THERAPY FOR INFANTS

PHILIP BANISTER *
M.B. Edin.

R. H. KAY
M.A., D.Phil. Oxfd

R. V. COXON
D.Phil. Oxfd, M.R.C.P.

From the University Laboratory of Physiology and the Radcliffe Infirmary, Oxford

THE appearance in Oxford of retrolental fibroplasia (retinopathy of prematurity) provided a stimulus for reviewing the whole question of the place of oxygen therapy in the management of premature infants (Bembridge et al. 1952). It was then agreed, after consultation among the various departments interested, that assessment of the progress of these babies would be greatly assisted if reasonably complete records could be secured of the level and duration of such therapy for each baby. For this reason it was proposed to install apparatus in the nursery which would automatically register the concentration of oxygen inspired by the infant at short intervals throughout the period of administration, and to record at the same time some objective measure of the infant's response. The first of these aims has now been realised, and some of the data obtained are reported here. It is hoped in the future to record also the oxygen tension in the infant's blood or tissues as an indicator of its response, but the considerable technical difficulties met with in this part of the project have not yet been entirely surmounted.

Material and Methods

The Infants

The general plan in the treatment of an infant requiring such nursing was to place it in the incubator as soon as

* Present address: Children's Memorial Hospital, Montreal 25, Quebec.

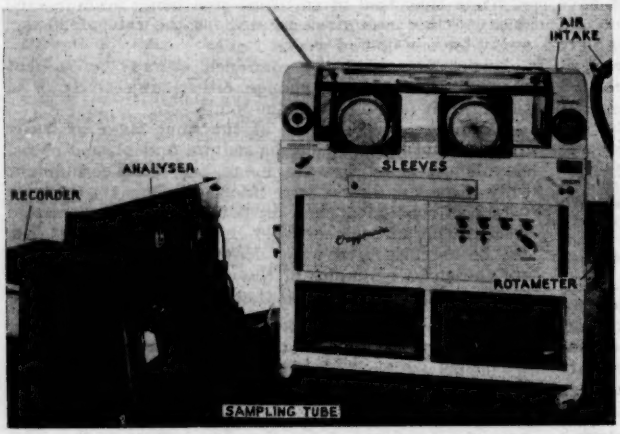

Fig. 1—Oxygenaire incubator with analyser and recorder.

possible after delivery, any necessary resuscitative measures being instituted after, rather than before, transfer to the apparatus. Since our recording equipment had been connected up before introducing the baby, the charting of the oxygen concentrations to which it was exposed could in this way be dated from the start of treatment. Not all the babies nursed in the incubator received added oxygen, but where this was deemed necessary by the physician-in-charge complete records could be obtained.

The Incubator

The incubator was supplied by the Oxygenaire Company and, with the coöperation of the manufacturers, has been somewhat modified in the following respects :

(1) Air was admitted through a long tube from outside the building, and a slightly larger circulating fan than that originally supplied was fitted.

(2) A ' Rotameter ' graduated to deliver 100–5000 c.cm. a minute was used to measure the inflow of oxygen. To use this it was necessary to widen the original inlet because the flow-gauge fitted by the maker depended on having a narrow jet at this point, which would have interfered with the calibration of the rotameter. When checked with the enlarged inlet the rotameter actually delivered 1030 c.cm. a minute at 17·5°C when set at 1000 ml. a minute and 5290 c.cm. a minute when set at 5000 ml. a minute.

(3) Through the courtesy of Mr. Gibbon, of Air Shields Inc., we were presented with a set of iris-type entry-ports as used in the ' Isolette ' and these were fitted to the English incubator.

The incoming air, mixed with oxygen admitted through the rotameter, enters the incubator at the "head" end, and the orifice of the plastic sampling tube was sited close to the infant's face. In the case of very active infants this relationship was not always maintained, but in practice sampling from the opposite end did not give very different figures. From the sampling tube the mixture of gases is sucked continuously at a rate of about 250 c.cm. a minute into the analyser.

The Analyser

The instrument used for analysis of the gas stream was built by the Cambridge Instrument Company and incorporates two katharometers, one measuring oxygen and the other carbon dioxide. The sample, which is drawn through the meters by an electrically driven pump, must first be well dried, because in the presence of moisture the recorded oxygen content is too high. Since the humidity in the incubator is very high, most of the moisture is condensed out in a trap surrounded by iced water. The remaining moisture is extracted from the air by passing it over calcium chloride.

The principle of the katharometer (Shakespear 1920) is that the mixture of gases to be analysed is brought into contact with a heated platinum wire so arranged in a closed chamber that the heat lost from the wire is related to the thermal conductivities of the gases surrounding it. Since the electrical resistance of the wire is in turn related to its temperature, the composition of a mixture of gases can be determined so long as the thermal conductivities of its components differ sufficiently from one another. In practice the platinum wires, which are heated by a 12 V car battery, are incorporated into a Wheatstone-bridge circuit, two limbs being in contact with the gas to be analysed, and two in contact with a reference gas. The bridge is balanced to zero when the concentrations of oxygen and carbon dioxide in the entering gas are those found in outside air. At other concentrations the off-balance currents give a measure of the excess of oxygen or carbon dioxide present over that found in air, and this is recorded with a Cambridge two-channel recording milliammeter on a 24-hour-strip chart. The oxygen is recorded on two ranges covering 21–50% and 21–80%, and the carbon dioxide from 0 to 10%. An adjustment is included in the electrical circuit to compensate for the different argon contents of atmospheric air and cylinder oxygen. Provided the instrument's reading is checked against air before and after each day's run, the accuracy attainable ranges from a fraction of 1% at 20% oxygen to about ± 1% at 50% oxygen and is about ± 2% at 80% oxygen. Drift in the instrument, when properly adjusted, does not exceed the equivalent of 0·5% oxygen for a constant concentration of the gas. Recordings of carbon-dioxide concentrations are accurate to about ± 0·1% ; as in the case of oxygen, this represents the performance of the instrument in use, and, since this was judged adequate for the present purpose, no serious attempt was made to improve on it. The instrument was calibrated with the aid of a Pauling oxygen-meter (modified Beckman model ' S ') and a Haldane apparatus. Since the gas passes into the analysing chambers of the katharometers by diffusion, the response time of the katharometers is rather long—i.e., about 4 minutes. (The recording arrangements and their calibration will be described more fully elsewhere.)

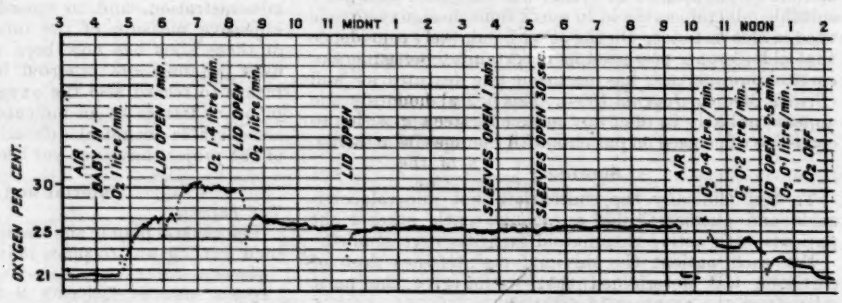

Fig. 2—Oxygen history of baby delivered by cæsarean section, showing effect of opening lid of incubator.

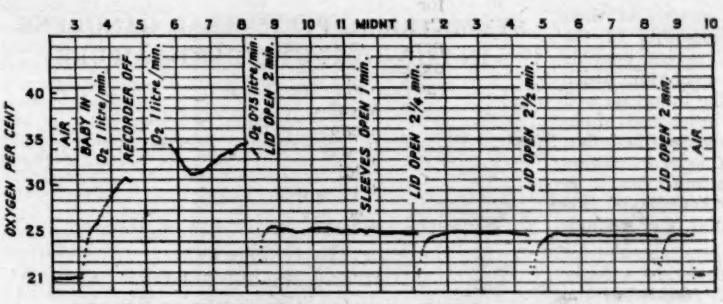

Fig. 3—Record from another case showing effect of opening lid of incubator.

Results

MODIFIED 'OXYGENAIRE' INCUBATOR

Fig. 1 shows the recorder and incubator set up in the nursery.

Oxygen

Fig. 2 is an example of a record of the complete "oxygen history" of a baby delivered by cæsarean section because of maternal toxæmia and admitted to the incubator (which at that time contained air) in good condition very soon after birth. Cyanosis was the indication for giving oxygen. The figure shows that the biggest concentration measured was 30%, and that the level was maintained at 26% during the night, the flow being tailed off next day. Both this record and that seen in fig. 3, from another case, show the effect of opening the incubator lid on the concentration; this can be compared with the insignificant effect caused by giving the same nursing attention through the sleeves (fig. 1).

At the Radcliffe Infirmary the oxygen is supplied to the nursery through a pipe from the main hospital bank. This is a new type of arrangement, incorporating a

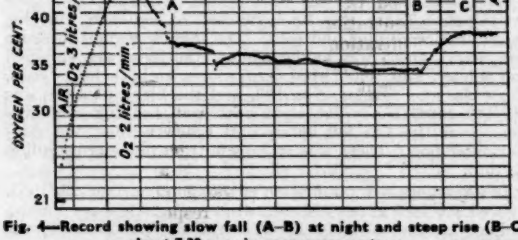

Fig. 4—Record showing slow fall (A–B) at night and steep rise (B–C) about 7.30 a.m. in oxygen percentage.

reservoir of liquid oxygen, and eliminates the necessity of changing cylinders; hence there is practically no chance of a failure of supply. Even so, fluctuation of the flow does arise and has not yet been entirely controlled, although it has been less since the input pressure was raised from 40 to about 60 lb. per sq. in.

Fig. 4 shows a slow fall during several hours in the night (A–B in figure) followed by a steep rise about 7.30 A.M. (B–C in figure). These changes took place without any alteration in the settings of the controls on the incubator. The changes are real since, as mentioned above, the long-term drift in the analyser has been not more than 0·5% of oxygen.

Carbon Dioxide

Tracings of carbon-dioxide concentration have been omitted from the accompanying charts for the sake of clarity since they revealed no important short-term changes. The level of carbon dioxide in the incubator never exceeded 0·2%, which is consistent with the results of several isolated Haldane analyses.

OTHER METHODS OF ADMINISTRATION OF OXYGEN

Covered Cot

Fig. 5 was obtained from an unoccupied metal cot similar to that described by Crosse (1952) but incompletely covered by a plastic lid wedged open 2½ inches; such an arrangement was at one time in use at Oxford and elsewhere. The fluctuations seen on this oxygen record correspond to the setting up of air currents in the nursery when the door was opened.

Funnel

Records made by placing a sampling tube alongside the mouth of an infant receiving oxygen by funnel during short periods of emergency have been very variable, but oxygen readings as high as 60% have been seen with

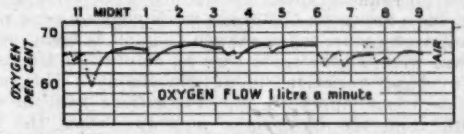

Fig. 5—Record of oxygen percentage in an unoccupied metal cot with plastic lid wedged open 2½ inches.

the gas flowing at 1 litre a minute, and the carbon dioxide has been more than 1% at times.

Queen Charlotte Tent

Although the use of this apparatus was discontinued at the Radcliffe Infirmary some considerable time ago, it is of interest in retrospect that a flow of 1·5 litres a minute has been shown to produce a concentration of oxygen exceeding 55% in this type of container.

Discussion

A few years ago the routine use of oxygen in the care of premature infants was orthodox practice (Anderson 1950), but misgivings followed the recognition of blindness due to retrolental fibroplasia as a complication of prematurity, and of the possible connection between this blindness and oxygen therapy (*Lancet* 1954). Yet the nature of the connection between eye lesions and oxygen has been variously interpreted: a consideration of clinical histories led some workers—e.g., Campbell (1951) and Gordon et al. (1954)—to regard exposure to high concentrations of oxygen as the prime cause, whereas Szewczyk (1953) is inclined to blame relative anoxia during withdrawal of the baby from an oxygen-enriched atmosphere. However, recent experiments made by Ashton et al. (1954) have clearly shown the deleterious effects of high concentrations of oxygen on the eyes of newborn kittens.

A great difficulty in attempts to assess the effects of oxygen therapy on infants is that information on the quantity of oxygen given is usually scanty or nil. Far-reaching conclusions thus tend to be drawn from very fragmentary information about the mixture breathed, since such information is generally derived either from scattered analyses or from simple flow-meter readings which, in many instances, give a very poor indication of what the baby is inhaling.

It therefore seems that the compilation of reasonably complete oxygen histories of premature babies could be

of the utmost value in retrospective surveys of their progress. At the same time the availability of the record for scrutiny during treatment makes possible exact control of the conditions in the incubator, which may be of some immediate benefit to the infant as well as a source of reassurance to those in charge of its management. We also propose, as opportunities offer, to secure records from such sick full-term infants as receive oxygen on various indications, for it is possible that, as with prematures, the benefits of this treatment may have been exaggerated and require reassessment.

We hope in time to accumulate and review a fairly large number of such oxygen histories. Meanwhile the records reproduced here illustrate certain points which deserve emphasis. The relatively constant conditions which can be attained with a suitably designed incubator such as that depicted in fig. 1 are a considerable advantage in themselves, and the use of the accurate rotameter fitted to it allows fine regulation of the flow when the infant is being weaned from oxygen. The fluctuations observed in the record from a Sorrento cot (covered by a partly open lid) when the nursery door was opened or when air currents were generated form a striking contrast with the constancy of the conditions in the closed incubator. These fluctuations merit some attention, since Szewczyk (1953) has recommended some such open-lid procedure when oxygen therapy is being withdrawn, while at the same time he emphasises the need for avoiding variations in oxygen supply. The same considerations apply to the fluctuations seen in the record from the Oxygenaire incubator when the lid, instead of the sleeves, is opened to attend to the baby. Although the administration of oxygen through a funnel is often considered inefficient and may be so as regards adults, in the case of infants our results indicate that high concentrations can be attained thereby. This may be due to the fact that the infant's small face sits well into the funnel, while its pulmonary ventilation is small compared to the oxygen-flow rate. At all events, when oxygen is given through a funnel, higher levels have been observed than that which Ashton et al. (1954) found to produce retinal change in kittens. This level is also exceeded in records from the Sorrento type of cot when covered.

Although Ashton et al. (1954) found no changes in the eye of kittens exposed to atmospheric concentrations of carbon dioxide up to 5%, Cross et al. (1953) have shown that levels of 0·5% will induce change in respiratory pattern in premature infants. The latter figure was reached in the inspired air during administration of oxygen by funnel but not in the Oxygenaire incubator.

Summary

An instrument is described which has been used for obtaining continuous records of the oxygen concentration in gas mixtures administered to infants.

Records are presented of the concentrations obtaining under certain conditions of administration.

The value of such records in the follow-up of treated infants is discussed together with some implications of the preliminary findings.

We wish to thank Dr. Victoria Smallpeice for her constant help and encouragement; the obstetricians at the Radcliffe Infirmary for permission to work in the nursery there; Mr. A. C. L. Houlton, for facilities in connection with the ophthalmic follow-up of premature babies; Sister R. K. Ware and her nurses for their invaluable coöperation; the Superintendent and staff of the Admiralty Research Laboratory for their help in connection with the Pauling analyser; Mr. J. L. M. Holle, lately of the Oxygenaire Company, for modifications to their incubator; and Mr. A. Austin for the photography.

References at foot of next column

SYMMETRICAL PERIPHERAL GANGRENE IN LOW-OUTPUT HEART-FAILURE

T. BIRD
M.D. Durh.
LECTURER, DEPARTMENT OF PATHOLOGY

C. S. LEITHEAD
M.B. St. And.
CLINICAL ASSISTANT, DEPARTMENT OF MEDICINE

K. G. LOWE
M.D. St. And., M.R.C.P., M.R.C.P.E.
SENIOR LECTURER, DEPARTMENT OF MEDICINE

UNIVERSITY OF ST. ANDREWS

IN low-output heart-failure blood-flow is not equally reduced in the various vascular beds of the body. There is thus an "order of sacrifice" (Franklin 1951) whereby the myocardium and the central nervous system are relatively well supplied with blood, while some of the abdominal organs, notably the kidneys and liver, have considerably reduced blood-flow, and the limb muscles and skin are very severely deprived. Differences in vasoconstrictor tone between the various arteriolar beds are thought to account for the unequal reductions in organ blood-flows. In some patients vasoconstriction may be so severe in the digits, nose, and ears as to lead to gangrene (Fishberg 1940). Such peripheral gangrene of strikingly symmetrical distribution has been recorded most often in patients with either left auricular ball thrombus (with or without mitral stenosis) or myocardial infarction. In the case reported here peripheral gangrene developed terminally in a patient with myocardial infarction.

Case-report

A man, aged 65, was admitted to the Royal Infirmary, Dundee, on Dec. 23, 1953. He had been breathless on exertion for several years, and six months previously he had been treated for hypertension and congestive heart-failure. Since then he had had occasional attacks of giddiness, and for three weeks before admission had intermittent gnawing pain across the front of his chest, unrelated to exercise.

On examination he was orthopnœic, lethargic, and very emotional. There was no cyanosis of mucosæ, but his extremities were blue and cold. The jugular venous pressure was raised, there was ankle œdema, the liver was enlarged and tender, and there were crepitations at both lung bases. The pulse was regular, rate 100, and the blood-pressure was 210/140 mm. Hg. The apex-beat was heaving and was located in the 6th left intercostal space beyond the mid-clavicular line. There was an intermittent parasternal gallop rhythm.

Investigations.—Examination of the blood on Dec. 23, 1953, showed Hb 10·5 g. per 100 ml., white cells 23,500 per c.mm., and polymorph leucocytosis. The urine on Dec. 24, 1953, was acid and contained much protein; and electrocardiography showed normal rhythm and Q R S, and T-wave inversion in leads I, aV_L, V_4, and V_5. On Dec. 25, 1953, the blood-urea level was 146 mg. per 100 ml., plasma-bilirubin level 0·5 mg. per 100 ml., plasma-albumin level 2·85 g. per 100 ml., plasma-globulin level 3·05 g. per 100 ml., alkaline phosphatase 30 King-Armstrong units per 100 ml., cephalin flocculation

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+++, and thymol turbidity +. Chest radiography on Dec. 25, 1953, showed generalised cardiac enlargement and shadows consistent with pulmonary œdema extending from the hila. On Dec. 28, 1953, the blood-urea level was 350 mg. per 100 ml.

Fig. 1—Well-demarcated gangrene of the nose two days before death.

Progress.—The patient became increasingly drowsy and orthopnœic and gradually developed Cheyne-Stokes respiration. Some improvement was obtained with intravenous aminophylline, but this was always temporary. His extremities continued to be strikingly cold and showed steadily increasing cyanosis. By the time of death on Dec. 29, 1953, there were clearly demarcated gangrene of the nose (fig. 1) and incipient gangrene of all the fingers and of the first four toes on each foot (fig. 2). The ears were warm initially and later showed no changes comparable with those in the digits.

Necropsy (twenty hours after death).—Externally the features of note were the well-demarcated gangrene of the end of the nose and the intense cyanosis of all the fingers and of the first four toes of each foot, the little toes being normal. Vesiculation and superficial ulceration were seen on the dorsal surfaces of the big toes. The cyanosis extended to the base of the phalanges, where it stopped abruptly. The ears and lips were not cyanosed. There was slight œdema of the legs and sacral area but no free fluid in the body cavities. There was no jaundice. The heart was greatly enlarged (680 g.) mainly as the result of hypertrophy and dilatation of the left ventricle, whose wall was 2·2 cm. thick at the base. There was a small and firmly adherent mural thrombus on the posterior wall of the left ventricle over an infarct involving an area of the inner half of the myocardium and measuring about 3 × 3 cm. No thrombus was seen in the other chambers. The right ventricular myocardium was thickened to 0·7 cm. The coronary arteries showed moderate calcific atheroma, and thrombus was present in the circumflex branch of the left coronary artery. The lungs were heavy (right 1000 g., left 750 g.) with œdema; there was early hypostatic pneumonia in the lower lobes; the pulmonary arteries were normal. The liver was slightly enlarged (1700 g.) and engorged, with a "nutmeg" appearance. The spleen was congested but not unduly firm. The kidneys were small, together weighing 150 g., with a coarsely granular surface and an irregularly thinned cortex with prominent thick-walled vessels. The remaining viscera were normal. The aorta and its main branches showed only moderate atheroma with no calcification, and detailed dissection of the arteries of the upper and lower limbs showed only moderate irregular thickening, with no calcification, and with no evidence of thrombus. The large veins revealed no abnormality.

Fig. 2—Gangrenous change in toes at death.

Microscopy confirmed the pulmonary œdema and early pneumonia. The infarct in the left ventricle was of about seven days' duration, with an overlying thrombus showing some organisation of the base. There was patchy fibrosis in the remainder of the myocardium but no recent necrosis apart from the infarct. The liver showed sharply defined coagulative necrosis of the hepatic cells of the inner fourth of the lobules, with slight hæmorrhage only at the periphery of the affected zones and little or no sinusoidal dilatation in the remainder of the lobules. No disturbance of reticulin pattern was seen in the necrotic areas, and the changes appeared to be of recent origin. The kidneys showed the changes of advanced hypertensive nephrosclerosis, with much destruction and fibrosis of renal tissue, but the surviving tubules were well preserved, with no evidence of recent necrosis. The third and fifth toes of each foot were removed and examined by repeated cross-sections. There was slight intimal thickening and medial fibrosis in the digital arteries, but little dimunition of the lumina. The arteries were well filled with erythrocytes, among which were entangled white cells and strands of fibrin (acid picro-Mallory method; Lendrum 1949). Nowhere was there any endothelial reaction; and, though the appearances were acceptable as those of thrombosis, it seemed unlikely that this had been present for more than a day or so. There was no evidence of œdema. In the third toes, however, the subcutaneous tissues showed fragmentation and deeply eosinophilic staining of the collagen fibres, and there were degenerative changes in the overlying epidermis. Histological examination of the gangrenous nose and fingers was, unfortunately, not permitted. Sections from other viscera and from cerebral cortex, basal ganglia, cerebellum, brain-stem, and spinal cord revealed no abnormality.

Discussion

The association of symmetrical peripheral gangrene with severe heart-failure of low-output type was described by Fishberg (1940), who said that it was "angiospastic in origin and the unfortunate side-effect of a compensatory mechanism." The condition is probably quite common despite the paucity of clinical reports in the past thirty years, because it is described in several textbooks, the authors referring to their own unpublished cases (Bull 1953, Fishberg 1940, Friedberg 1949).

Angiospastic gangrene of the nose can be simulated by gangrene due to embolism of a nasal artery in subacute bacterial endocarditis (Lutembacher 1917, Cockayne and Wilton 1941), but this is usually associated with embolism elsewhere. Ergot poisoning can cause gangrene of nose, extremities, and viscera (Wright 1948). Arterial thrombosis or embolism in patients with pneumonia is another cause of peripheral gangrene (Uhr 1938, Chatterjee 1940, Storstein 1951). In frost-bite exposed extremities become gangrenous, and other well-recognised causes of peripheral gangrene are thromboangiitis obliterans, severe arteriosclerosis, peripheral vascular disease in diabetes, scleroderma, Raynaud's syndrome, and polyarteritis nodosa.

From the clinical and necropsy findings it appears that gangrene in our patient was due to intense vasoconstriction in terminal low-output heart-failure. The symmetry was very striking, even to the extent of sparing both little toes.

Reduction in liver blood-flow may have been responsible in part for the recent well-localised centrilobular necrosis of the liver. The kidneys, however, showed no histological evidence of tubular epithelial damage; hence there must have been sufficient renal blood-flow to meet the kidneys' metabolic requirements. Nevertheless there must have been considerable reduction of renal blood-flow and glomerular filtration-rate to account for the considerable rise in blood-urea level—i.e., there was circulatory renal

insufficiency ("extrarenal uræmia"). Our patient was incontinent terminally, and the rate of urine flow was not known.

Summary

The case is reported of an elderly man with myocardial infarction, clinical features of low-output heart-failure, and the terminal development of symmetrical gangrene of nose, fingers, and toes.

The pathogenesis and differential diagnosis of this symmetrical peripheral gangrene are briefly discussed.

We are grateful to Prof. I. G. W. Hill for permission to publish, to Professor Hill and Prof. A. C. Lendrum for help with the manuscript, and to Mr. F. M. Duncan for the photographs.

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THE DESIGN OF INSULIN TRIALS

A POLYLYSINE INSULIN

G. R. FRYERS
M.D. Leeds, M.R.C.P.
SENIOR MEDICAL REGISTRAR

RONALD G. PALEY
M.D., Ph.D. Leeds
RESEARCH FELLOW

R. E. TUNBRIDGE
O.B.E., M.D., M.Sc. Leeds, F.R.C.P.
PROFESSOR OF MEDICINE

DEPARTMENT OF MEDICINE, UNIVERSITY OF LEEDS

THE control of diabetes should ensure a sense of well-being, a steady weight, freedom from hypoglycæmia and ketosis, and the maintenance of normoglycæmia (Tunbridge 1953). In addition to dietary measures insulin is necessary for the satisfactory control of most patients. To obtain a more uniform action and to minimise the number of daily injections several modifications designed to retard the action of insulin have been introduced. No generally accepted comparative assessment has been made of the commonly used retard insulins, such as protamine zinc insulin (P.Z.I.) and globin zinc insulin. Recently, more modified insulins have been developed, thus threatening further confusion unless their actions are rapidly and reliably assessed.

A therapeutic trial of any drug demands:

(1) A study of a homogeneous group of patients. Conclusions might be invalidated if a small proportion of patients from the main group reacted in an atypical manner to the drug under test.

(2) The basing of comparisons on those features of the disease which best reflect the action exerted by the drug.

(3) An experimental design that will ease statistical analysis.

In diabetes mellitus it is common clinical knowledge that there are two main groups of patients—the stable and the unstable—which appear clinically to be similar to the two groups described by Himsworth and Kerr (1939)—insulin-insensitive and insulin-sensitive. The stable diabetic shows only slight variation in the blood-sugar level, has almost complete freedom from glycosuria, and can be controlled without frequent hypoglycæmic reactions; his blood-sugar response to changes in insulin dosage is sluggish, and ketosis is almost unknown. On the other hand, the unstable diabetic is subject to large and erratic swings of blood-sugar levels, and glycosuria cannot be avoided without serious risk of hypoglycæmia.

It must be emphasised that no sharp demarcation separates the stable from the unstable patients. The term "brittle" should be reserved for the extremely sensitive group of patients showing a great day-to-day variability, and such patients are in consequence unsuitable for therapeutic trials.

In other studies patients for therapeutic trial of insulin have been selected by one of three methods:

(1) Random selection of all diabetics.

(2) Selection of patients with severe diabetes, the criterion of severity being the total daily dosage of insulin required to maintain control.

(3) Selection of diabetics whose blood-sugar levels could be kept about normal (stable diabetics).

The basis for comparing insulins has been extensively discussed by Crump (1952), who states that, in the past, most studies have used methods comparing the mean blood-sugar levels on various insulins, or the comparison of data collected on single days. Crump considers that the most important feature in the control of diabetics is the high variability of the blood-sugar level; he described two components of this variability:

(1) *Intra-daily variation* is the variability in the blood-sugar level during the twenty-four hours between injections. An insulin producing minimal intra-daily variation would be preferred.

(2) *Inter-daily variation* is the variability in the mean daily blood-sugar from one day to the next with the patient on the same dose of insulin.

Crump states that an insulin which controls intra-daily variation ideally might be quite unsatisfactory because of widely differing daily mean levels. A statistical analysis of intra-daily variation does not indicate a difference in the time of day for the occurrence of high or of low blood-sugar levels. Izzo and Crump (1950) therefore described the pattern of the intra-daily variation by plotting the mean deviation from the daily mean at specified times of day for each patient on each insulin.

The choice of an experimental design is never easy, and two methods are described. In both examples the statistical treatment is one of analysis of variance (Fisher 1946).

Methods

In both methods the patients were admitted to hospital, diet and exercise were rigidly controlled, insulin dosage was checked, and insulin was injected by a nursing sister or one of us. The times at which the blood-sugar level was measured were the same throughout each experiment. Capillary blood was used in both trials, and the blood-sugar level was estimated by the method of Hagedorn and Jensen (Harrison 1937).

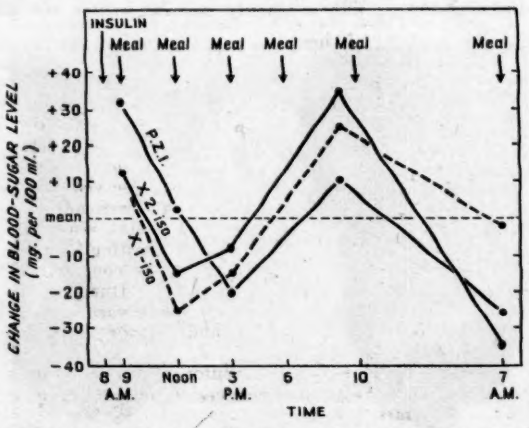

Fig. 1—Mean deviation from daily mean blood-sugar level of four patients on P.Z.I., insulin × one-isophane, and insulin × two-isophane.

METHOD I

The British insulin manufacturers recently organised a clinical trial of a new insulin, X, which is a polylysine insulin (patent application no. 24869/53). Four patients were selected on the basis of their being controlled by a single daily dose of P.Z.I., judged by seven days' preliminary observation. One of three insulins, labelled A, B, and C and all prepared from the same batch, was given until each had been randomly allotted on three even days. A was later revealed to be P.Z.I., B to be insulin X one-isophane, and C insulin X two-isophane. On the odd days known P.Z.I. was given, and the trial finished on an odd day. The random selection was done centrally. Finger-prick blood was collected five times on even days, at 7 A.M., 9 A.M., 11.30 A.M., 3 P.M., and 10 P.M., and once only, at 7 A.M., on odd days, for the estimation of blood-sugar.

Urinary sugar was estimated by Benedict's quantitative method. The patients were confined to the ward but not to bed. Mealtimes were the same for all the patients and were at 8 A.M., noon, 6 P.M., and 9 P.M. Their calorie intake was kept constant within the limits of ±50 calories a day. The patients were weighed daily, and no appreciable change was observed.

Results

Fig. 1 shows that insulin X one-isophane appears to have a more rapid action than P.Z.I. and insulin X two-isophane, and that, though the difference between P.Z.I. and insulin X two-isophane is slight, P.Z.I. appears to be somewhat slower in its action; this is best seen at midday and 3 P.M.

TABLE I—INSULIN REQUIREMENTS AND DIET

Method	Clinical details: Case no.	Sex	Age (yr.)	Duration of disease (yr.)	Insulin: Dose on admission (I.U.)	Type	Dose on trial (I.U.)	Diet: Carbohydrate (g.)	Fat (g.)	Protein (g.)
I	1	F	72	5	28	P.Z.I.	20	100	48	58
	2	F	53	19	40	P.Z.I.	40	123	56	68
	3	F	70	4	32	P.Z.I.	32	118	55	68
	4	M	71	11	24	P.Z.I.	24	155	79	82
II	5	F	31	4	64	1 : 1 sol. P.Z.I.	44	120	54	45
	6	F	36	4	40	,,	40	160	81	68
	7	F	48	15	48	,,	40	165	90	75
	8	F	32	4	40	,,	40	160	72	60

The means of the four patients' urinary excretions of glucose were 0·2, 0·1, 4·1, and 4·8 g. per twenty-four hours. Analysis of these results was uninformative.

METHOD II

Another four, all female diabetics, were selected because they were unstable patients and had no complications other than frequent hypoglycæmic attacks (table I). Their weights were remarkably steady during the period of investigation. The patients had been observed in the Diabetic Clinic at Leeds for some years and were admitted to the Diabetic Annexe, Pinderfields Hospital, Wakefield, for the trial. An initial period of review, lasting from one to two weeks, confirmed the satisfactory control on a 1 : 1 mixture of soluble insulin and P.Z.I. During initial testing remarkable constancy as regards variability of blood-sugar level was observed, and a longer period of adjustment was unnecessary.

The same strict routine being enforced as in the earlier experiment, the patients were investigated for four days with a 1 : 1 mixture of soluble insulin and P.Z.I. ready-mixed in the syringe. At the end of the four days a 1 : 1 mixture of soluble insulin and insulin X two-isophane ready mixed in the syringe was substituted. A period of adjustment lasting three days was allowed, and then for four days all the factors were kept as rigidly controlled as in the previous four days. Specimens of capillary blood were taken at 8 A.M., 11.30 A.M., 3.30 P.M., and 8 P.M.

TABLE II—BLOOD-SUGAR LEVELS

Method	Case no.	Blood-sugar (mg. per 100 ml.): On P.Z.I. Range	On P.Z.I. Mean	On X one-isophane Range	On X one-isophane Mean	On X two-isophane Range	On X two-isophane Mean
I	1	88–202	134	90–235	134	97–187	136
	2	88–212	135	82–217	130	65–259	136
	3	95–222	130	63–213	146	122–220	184
	4	63–213	136	120–188	154	93–218	155

Method	Case no.	On 1 : 1 mixture of soluble insulin and P.Z.I. Range	Mean	On 1 : 1 mixture of soluble insulin and insulin X two-isophane Range	Mean
II	5	78–368	219	145–434	221
	6	99–380	249	106–410	262
	7	77–430	297	97–404	275
	8	79–450	266	76–460	229

We were able, after the initial period of review, to maintain the individual insulin dosage constant throughout the whole study. No hypoglycæmic attacks occurred and there was no ketosis.

Results

The mass of data was so great that the presentation was difficult. The mean blood-sugar level and the range for each insulin and for each patient provided some information about the stability of the patients. No great difference was observed between P.Z.I. and insulin X. Table II reveals the vast range of blood-sugar levels observed but does not afford a satisfactory measure of variability. We therefore adopted the methods described above (Izzo and Crump 1950).

Table III shows the average values for intra-daily variation in blood-sugar levels for each patient on both insulins. Izzo and Crump found a ratio of variance ranging from 2 in non-diabetic patients to 5 in their diabetics. In the present study lower values were obtained with insulin X than with P.Z.I., but the differences were not significant.

The average values for inter-daily variation in blood-sugar levels are shown in table III. None of the differences were significant. The mean deviations from the daily mean of the blood-sugar level were analysed at the times selected. In this way the pattern of blood-sugar levels with various insulins can be compared.

Fig. 2 shows the pattern with a mixture of soluble insulin and P.Z.I. and for one of soluble insulin and insulin X two-isophane. The patterns are significantly

TABLE III—AVERAGE VARIATIONS IN BLOOD-SUGAR LEVELS

Variation	Case no.	On 1 : 1 mixture of soluble insulin and P.Z.I.	On 1 : 1 mixture of soluble insulin and insulin X two-isophane
Intra-daily	5	3·89	3·88
	6	4·46	4·29
	7	4·22	4·03
	8	4·44	4·20
Inter-daily	5	4·92	4·86
	6	3·43	4·04
	7	4·98	5·11
	8	4·68	5·13

The intra-daily and inter-daily variations measure the fluctuation in blood-sugar levels in a single day and over several days respectively. To measure these changes, monotonic functions of the variance of the readings have been used.

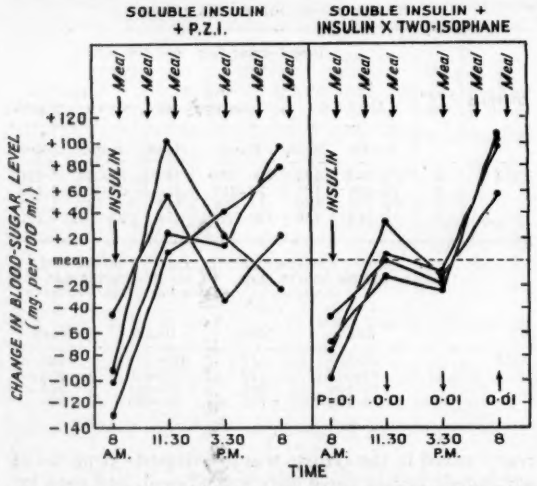

Fig. 2—Mean deviation from daily mean blood-sugar level of four other patients on 1 : 1 mixture of soluble insulin and P.Z.I. and on 1 : 1 mixture of soluble insulin and insulin × two-isophane. The lower arrows indicate the direction of the significant changes.

different. The points of difference indicated are as follows: no significant difference at 8 A.M.; and blood-sugar levels with insulin X significantly lower at 11.30 A.M. and 3.30 P.M., and significantly higher at 8 P.M.

Discussion

Izzo and Crump (1950) stated that stable diabetics were not ideal subjects for an insulin trial. Analysis of the data in method I showed insignificant difference between the insulins. Random selection of diabetics will include more stable than unstable patients; therefore the results of such an insulin trial are apt to be obscured by the results of the many.

Though method I allowed analysis of intra-daily variation of blood-sugar levels and the mean deviation from the daily mean blood-sugar levels for various insulins, *it precluded adequate analysis for inter-daily* variation of blood-sugar levels, and certainly did not allow for any carry-over effect of the longer-acting insulins. This is a serious criticism, since an insulin which controls intra-daily variation ideally might be quite unsatisfactory because of widely differing daily means.

A similar analysis of the data from method II showed no significant statistical differences, but the change in pattern of the mean deviation from the daily mean blood-sugar level in four unstable patients was significant. Thus the selection of an unstable group of patients brought into sharp focus the timing defects of the insulins under trial.

In following up the method, we found that one patient (case 3, Paley 1954) though continuously observed and appearing to be well controlled (that is to say, fulfilling all the ideal criteria), six months later gave a totally different response to insulin when the response was analysed critically. This variation in a patient who to all intents and purposes has behaved consistently, and in whom there had been no clinical deterioration, is a very serious stumbling block to rough and ready methods of the assessment of insulin action. This is, as far as we know, the first record of such a change in a person well controlled and completely stabilised in whom no new factor, such as infection, environmental stress, or other illness, could have been the cause. Furthermore, the alteration was not apparent until we did the detailed analysis. If these changes can occur in a controlled diabetic patient, it is quite obvious that we must be very much stricter in our criteria for assessing a new insulin.

The choice of an experimental design is never easy, and alternative methods to those presented could be designed. The advantages of the modification of Izzo's design that we have elaborated in method II are as follows:

(1) It takes account of all variations in the blood-sugar levels.

(2) It adjusts for possible carry-over effects which may alter with different modifications of insulins.

(3) It does not necessitate continuous estimations of blood-sugar level throughout the period of study.

(4) It allows the use of simple statistical analyses.

Summary

The general plan of insulin therapeutic trials is discussed, and two methods are described.

A method modified from that described by Izzo and Crump (1950) showed that in unstable diabetics the mean deviation from the daily mean blood-sugar level differed significantly from when they were receiving a 1 : 1 mixture of soluble insulin and P.Z.I.

It is suggested that the method, using unstable diabetics, where insulin timing is the more critical, should be used for the preliminary assessment of any new insulins, thus minimising confusion.

We wish to thank Dr. J. Adler and his assistant, Dr. D. A. Hall and his assistants, the ward sisters, the dietitian, and the patients for their willing coöperation in these therapeutic trials.

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THE DESIGN OF INSULIN TRIALS

INSULIN-ZINC SUSPENSION (LENTE)

RONALD G. PALEY
M.D., Ph.D. Leeds
RESEARCH FELLOW IN MEDICINE IN THE UNIVERSITY OF LEEDS

Hallas-Møller et al. (1951, 1952a, b, and c) suggested that the blood-sugar level could be satisfactorily controlled in difficult cases of diabetes with a single daily injection of the appropriate one of three insulin-zinc suspensions. Numerous papers have appeared recently reporting results obtained chiefly with insulin-zinc suspension ('Lente.')

Oakley (1953), comparing it with other insulin preparations, considered that it gave better results in 7 of 11 patients. He thought that insulin-zinc suspension was the most useful of the three new insulins.

Murray and Wilson (1953) found improved control with insulin-zinc suspension in 8 of 18 patients previously maintained on other preparations.

Nabarro and Stowers (1953) claimed that insulin-zinc suspension gave adequate control in 9 of 19 patients with severe diabetes.

On the other hand, FitzGerald et al. (1954) stated that when 30 patients with diabetes mellitus, of whom 24 were

TABLE I—INTRA-DAILY VARIATION OF BLOOD-SUGAR LEVELS ON P.Z.I.

Case no.	June	November
1	3·89	4·12
2	4·46	4·01
3	4·22	4·12
4	4·44	4·26

Monotonic functions of the variations of the readings have been used.

TABLE II—INTER-DAILY VARIATION OF BLOOD-SUGAR LEVELS ON P.Z.I.

Case no.	June	November
1	4·92	3·68
2	3·43	4·19
3	4·98	4·71
4	4·68	2·93*

* No significant differences noted. P = 0·1

considered to be indifferently controlled biochemically, were transferred from one type of insulin to an equal dose of insulin-zinc suspension, a third of them were less well controlled, and in half of them the control was unchanged.

Izzo and Crump (1950), in America, have devised a highly sensitive method of observing significant differences in insulin timing. The second method described by Fryers et al. (1954) was therefore used to assess the action of insulin-zinc suspension.

Appraisal of Control Periods

Four unstable diabetics, extensively studied six months previously in the first insulin trial (Fryers et al. 1954),

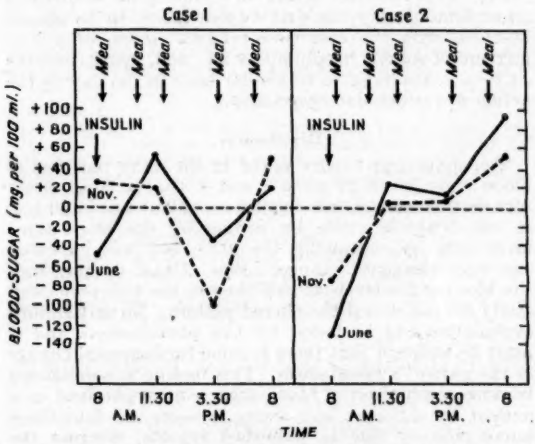

Fig. 1—Mean deviations from daily mean blood-sugar level in cases 1 and 2 in June and November.

were readmitted to the Diabetic Annexe, Pinderfields General Hospital, Wakefield, for trial with the new insulins. They had been kept under constant surveillance for the six months, and on admission their clinical states were unaltered and their daily insulin requirements were the same as in the previous trial. Nevertheless a week was allowed to see if any adjustment in treatment was necessary. None had to be made, and serial estimations of the blood-sugar levels indicated optimal control. The patients were kept under uniform conditions and after a week were subjected to a two-day trial on their established mixture of soluble and protamine zinc insulin (P.Z.I.). Their blood-sugar levels were estimated at 8 A.M., 11.30 A.M., 3.30 P.M., and 8 P.M.

The data obtained were then analysed for variance; table I shows no significant difference between the intra-daily variation of blood-sugar levels for the four patients on identical doses of insulin in two periods of observation separated by six months (June and November, 1953).

When the data are analysed for inter-daily variation of blood-sugar levels in June and November, though differences are noted none are significant (table II).

Fryers et al. (1954) have shown how total variability among the blood-sugar responses for each patient on each insulin may be divided into two components intra-daily and inter-daily variability. Izzo and Crump (1950) stated "that different modified insulins displayed no differential ability to control the extent of intra- and inter-daily variability of blood-sugar responses." This we have confirmed. The type of insulin, however, does influence the daily pattern of distribution of insulin activity; this pattern, expressed as the mean deviation from the daily mean blood-sugar level, is in our view the most informative finding that can be derived from the data. For instance, no significant difference between the curves for June and November in cases 1 and 2 is detected in fig. 1, whereas the curves in cases 3 (fig. 2) and 4 (fig. 3) for June and November show a significant difference.

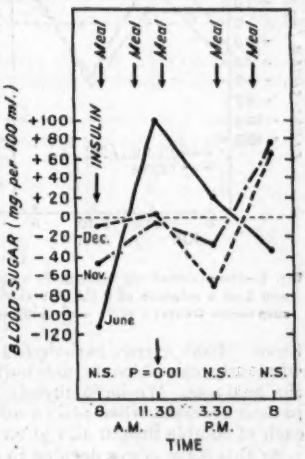

Fig. 2—Mean deviations from daily mean blood-sugar level in case 3 in June, November, and December. N.S., not significant.

No explanation is forthcoming from the experimental conditions for the differences, since the insulins were of the same batch in both trials, the doses were the same, the diet was identical, and the amount of exercise allowed was strictly comparable. Improvement in control during the trial cannot be held responsible, since the curves represent a similar degree of variation. The clinical experience with case 3 also tends to discount improvement in control as a cause of these differences: after severe hypoglycæmic episodes with insulin-zinc suspension during the trial, case 3 reverted immediately to the November pattern when placed on her accustomed dose of a mixture of soluble insulin and P.Z.I. and *not* to the June pattern (fig. 2).

Insulin-zinc Suspension

In the four patients the mixture of insulin was changed to insulin-zinc suspension. A period of adjustment was allowed; from determinations of the blood-sugar levels in the early days and at the end of the period a week appeared to suffice for this. No change had to be made in the individual insulin doses during this phase. No hypoglycæmic attacks occurred and there was no ketosis.

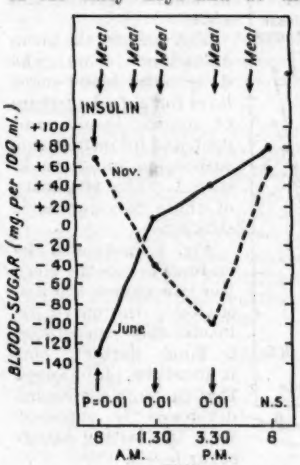

Fig. 3—Mean deviations from daily mean blood-sugar level in case 4 in June and November: N.S., not significant.

There then followed a four-day period in which all the factors remained as rigidly controlled as in the initial trial. No difficulties were encountered except in case 3, who had troublesome hypoglycæmic attacks between midnight and 3 A.M., which continued in spite of a reduction of the dose of insulin-zinc suspension from 40 to 32 units. Hypoglycæmia was so intense at

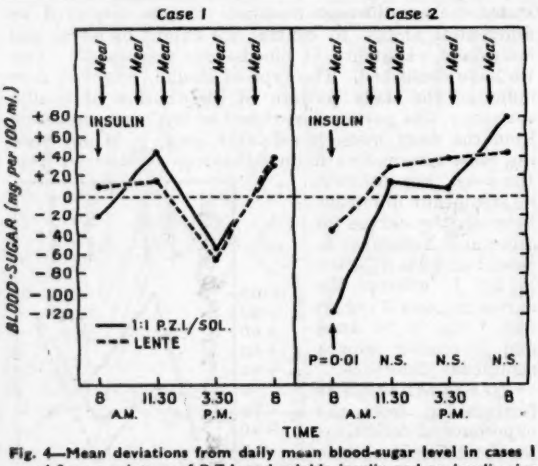

Fig. 4—Mean deviations from daily mean blood-sugar level in cases 1 and 2 on a mixture of P.Z.I. and soluble insulin and on insulin-zinc suspension (lente): N.S., not significant.

times that extra carbohydrate had to be given. Obviously case 3 could not be included in this part of the analyses. We have already shown how quickly this patient reverted when placed on her mixture of 20 units each of soluble insulin and of P.Z.I.

At this stage it was decided to extend the trials. Case 1 had been maintained on insulin-zinc suspension manufactured in Britain. She was now changed to insulin-zinc suspension manufactured in Denmark. Conversely, case 2 received the Danish insulin-zinc suspension originally and was now changed to the British insulin-zinc suspension. A period of three days was allowed for any adjustment to this change of brand of insulin-zinc suspension. There then followed a four-day test in which food, dose of insulin, and exercise were the same as in the previous four-day trial.

The findings in both patients were remarkably similar, revealing no difference between the action of British and Danish insulin in the two test periods. The results can therefore be grouped and compared with the grouped results obtained in the trials of a mixture of soluble insulin and P.Z.I.

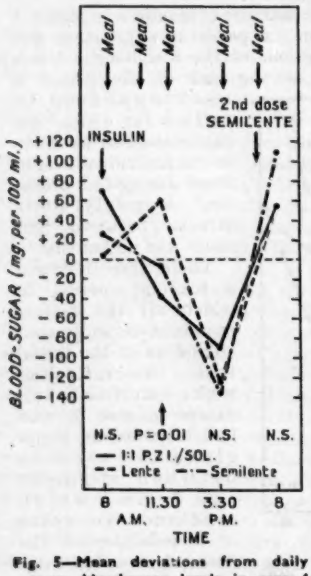

Fig. 5—Mean deviations from daily mean blood-sugar levels in case 4 on a mixture of P.Z.I. and soluble insulin and on insulin-zinc suspensions (lente) and (semilente).

Fig. 4 shows the mean deviations from the daily mean blood-sugar level for a 1 : 1 mixture of soluble insulin and P.Z.I. and for insulin-zinc suspension obtained in case 1. The similarity of these two curves is striking.

Fig. 4 shows also the findings in case 2. Here the two curves are dissimilar: the curve for insulin-zinc suspension is much flatter; but it must be emphasised that the only significant difference is observed with the fasting blood-sugar levels.

The findings in case 4 show that insulin-zinc suspension does not alter control dramatically, although it does significantly raise the blood-sugar level at 11.30 A.M. It is seen that the 3.30 P.M. fall and the 8 P.M. rise of blood-sugar levels are almost identical for insulin-zinc suspension and for the mixture of soluble insulin and P.Z.I. (fig. 5).

Insulin-zinc Suspension Amorphous

Since insulin-zinc suspension contains 30 parts of insulin-zinc suspension amorphous ('Semilente') and 70 parts of insulin-zinc suspension crystalline ('Ultralente'), in case 4 the dose of 40 units of insulin-zinc suspension can be broken down to 12 units of insulin-zinc suspension amorphous and 28 units of insulin-zinc suspension crystalline.

It was therefore decided to observe the effect of two doses of insulin-zinc suspension amorphous—one given before breakfast and the other before supper. According to Gerritzen (1953) the action of insulin-zinc suspension amorphous resembles that of globin zinc insulin and N.P.H. insulin. After a preliminary adjustment period a further four days' trial was made with insulin-zinc suspension amorphous 20 units before breakfast and 8 units before supper.

Fig. 5 shows the action of insulin-zinc suspension amorphous during the first twelve hours to be almost identical with the first twelve hours' action of a 1 : 1 mixture of soluble insulin and P.Z.I., and, apart from the 11.30 A.M. readings, to be similar later in the day to the action of insulin-zinc suspension.

Discussion

The significant change noted in the daily patterns of blood-sugar levels in cases 3 and 4 after a lapse of six months was unexpected. Careful surveillance at 11.00 A.M. in the Diabetic Clinic by estimating the blood-sugar levels and by examining the urine had not indicated any such dramatic change. Figs. 2 and 3 show that the blood-sugar levels at this time in the two periods of study did not reveal the altered pattern. No satisfactory explanation can be found for this phenomenon, and it must be assumed that there is some fundamental change in the patient's metabolism. This finding is emphasised because comparison of blood-sugar curves obtained in a patient by different long-acting insulins are sometimes found side by side in published reports, whereas the period of observations may be separated by as much as a year.

In comparing the effect of any new insulin, the juxtaposition of trial periods seems to be imperative; otherwise the effect of the time interval between studies may either mask or accentuate the real effect produced by an insulin.

Gerritzen (1953) places insulin-zinc suspension in a group of insulins whose action lasts sixteen hours and is greatest from five to seven hours after administration. He considers that, among the insulins of this class, insulin-zinc suspension has the smoothest action. With insulin-zinc suspension the first fall in blood-sugar level is observed in the early afternoon, and Oakley (1953) states that nocturnal reactions are uncommon and that hypoglycæmia rarely develops in the early hours of the morning. Case 3 had repeated attacks of hypoglycæmia from midnight to 3 A.M.; these were so severe that she had to be excluded from the trial.

Case 1 (fig. 4) shows remarkably constant curves with the insulin mixture and with insulin-zinc suspension. Case 1 was selected in June, 1953, because she was known to be of an unstable type. These curves, however, are similar to those presented by Izzo and Crump (1950), who tested many insulins in stable diabetics. Case 1 thus seems to fall in the hinterland of the stable and unstable diabetics. Such curves render it impossible to state whether insulin-zinc suspension is a superior insulin or not.

On the other hand, case 2 was ideal to demonstrate the smoother action of insulin-zinc suspension (fig. 4). Case 4 (fig. 5), however, hardly supports this thesis, and the 11.30 A.M. rise of blood-sugar level with insulin-zinc suspension does not add to the smoothness of its action. Possibly the addition of insulin-zinc suspension crystalline might have rendered the action smoother.

From this very detailed study it seems that the insulin-zinc suspension preparations suffer from the same limitations as do other insulins.

It has been shown that the type of insulin can influence the daily pattern of insulin activity, but it cannot control the stability or, in other words, the extent of the variability of blood-sugar responses.

Summary and Conclusions

The usefulness of the method of insulin trials originally described by Izzo and Crump and modified by us is confirmed.

The tests should be made consecutively with a minimum of delay between trials.

The new insulin-zinc suspensions—amorphous, crystalline, and mixtures—appear to suffer from the same limitations as do other insulin preparations.

I wish to thank Dr. J. Adler and his staff for the many blood-sugar determinations, and the ward sisters and dietitians for their help. Boots Pure Drug Co. Ltd. and Evans Medical Supplies Ltd. supplied the preparations of insulin.

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TREATMENT OF VENOUS THROMBOSIS WITH ANTICOAGULANTS

REVIEW OF 1135 CASES

JOHN MARKS
M.A. Camb., M.D. Lond., M.R.C.P.
UNIVERSITY ASSISTANT PATHOLOGIST TO ADDENBROOKE'S HOSPITAL, CAMBRIDGE

B. M. TRUSCOTT
M.B.E., M.A. Camb., M.B. Lond., F.R.C.S.
CONSULTANT SURGEON, UNITED CAMBRIDGE HOSPITALS

J. F. R. WITHYCOMBE
M.A., M.Chir. Camb., F.R.C.S.
COMYNS BERKELEY BYE-FELLOW, GONVILLE AND CAIUS COLLEGE, CAMBRIDGE

SINCE the excellent accounts of the use of heparin and other anticoagulants in venous thrombosis by Bauer (1946), Ball and Hughes (1949), and others this therapy has been widely used. In this general hospital of 500 beds and in the district around it more than 1200 cases have received such treatment during the past five years; the results are reviewed here.

Treatment of venous thrombosis aims at reduction in its morbidity and at elimination of mortality from massive pulmonary embolism. The morbidity has been successfully reduced, as the rapid relief from pain, the shorter period of rest, and the early subsidence of leg swelling have shown. Deaths from pulmonary embolism, however, have continued to take place, most of them without any symptoms or signs before the massive and rapidly fatal embolism and therefore untreated.

Cambridge Method of Treatment of Venous Thrombosis

PRINCIPLE

Treatment with anti-prothrombin drugs has been combined with an initial course of intramuscular heparin.

In the early stages of the present study dicoumarol was given, but it has now been superseded by either ethyl biscoumacetate or phenylindanedione, which substances reduce the coagulability of the blood within about twenty-four hours to a level at which further thrombosis is unlikely.

Heparin is given to cover the first twenty-four hours during which time the anti-prothrombins are not effective.

The main features in the course of treatment are illustrated in fig. 1.

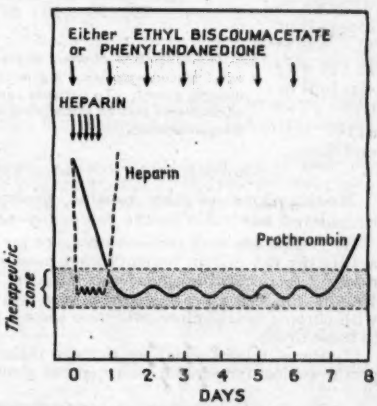

Fig. 1—Diagram illustrating combined use of heparin and anti-prothrombin drugs. Therapeutic zone represents coagulation-time of 15–25 minutes and prothrombin content of 10–25% of normal.

METHOD

When venous thrombosis has been diagnosed, the laboratory is informed, and treatment is started immediately with anticoagulants according to the following plan:

First Day

The patient is confined to bed. Since the pain is sufficient to discourage activity, no steps (such as splinting the leg) are taken to limit movement.

An injection of heparin 150 mg. with hyaluronidase 0·1 mg. is given through a fine needle into the muscles of the outer aspect of the thigh. Intramuscular injection of heparin is painful, causes local bruising, and is absorbed at variable rates. These disadvantages are overcome by using hyaluronidase.

This initial dose is followed by 50 mg. of heparin (and 0·1 mg. of hyaluronidase) four-hourly for four doses.

At the time of the first injection of heparin the patient is given either ethyl biscoumacetate 1·2 g. or phenylindanedione 250 mg. by mouth.

Subsequent Days

No further heparin is given. A sample of blood is taken daily, and the prothrombin-time is estimated by a one-stage method. The dosage with anti-prothrombin agents is regulated by this result. No fixed rules are possible for dosage, for it is based on the trend in "prothrombin level" (see below) rather than on the absolute value. Treatment aims at maintaining the "prothrombin level" between 10% and 25% of the average normal value.

The average maintenance dose may be calculated from the following table:

Prothrombin content	*Dose* *Ethyl biscoumacetate (g.)*	*Phenylindanedione (mg.)*
Less than 15%	Nil	Nil
15–25%	0·15	50
26–35%	0·3	100
36–45%	0·45	
46–55%	0·6	150
More than 55%	0·75	200

Active exercise in bed is encouraged as soon as pain disappears. When the leg is no longer tender, the patient is allowed up. If œdema persists after three days, an elastic bandage is applied until it subsides.

After pulmonary embolism without obvious venous thrombosis the stage at which the patient can be allowed up is more difficult to assess, but the usual interval was four or five days after the embolism.

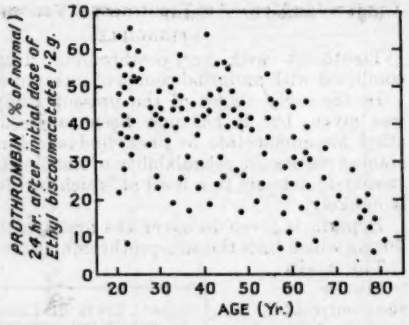

Fig. 2—Correlation of effect of standard initial dose of ethyl biscoumacetate 1·2 g. with age of patient (no heparin given). To patients aged more than 60 it is advisable to give an initial dose of only 0·9 g. of ethyl biscoumacetate.

MODIFICATION OF TREATMENT

Modifications of the routine described above are considered advisable in the following conditions:

(1) Old people have reduced tolerance for anti-prothrombin agents (fig. 2), and in patients aged more than 60 an initial dose of either ethyl biscoumacetate 0·9 g. or phenylindanedione 150–200 mg. was given. A similar dose was given to patients with chronic heart-failure, who also show a reduced tolerance to these drugs.

(2) Renal failure and liver damage make the use of anti-prothrombins undesirable, and heparin alone should be used.

TREATMENT OF OVERDOSAGE

Although overdosage of these drugs has rarely been seen in this series, methods are available for limiting any overdosage or for returning a low value to normal for subsequent urgent operations.

(1) *Overdosage with heparin* can be overcome with an intravenous injection of 5–10 ml. of a sterile 1% solution of protamine sulphate.

(2) *Overdosage with anti-prothrombins.*—Vitamin-K_1 oxide produces a variable effect but will often accelerate the rate of recovery from overdosage with ethyl biscoumacetate (Stirling and Hunter 1951).

We have tried the effect of vitamin K_1 100 mg. by mouth on 25 patients at the end of their treatment: 10 showed a rise of more than 10% in the prothrombin content during the following four hours, 7 a rise between 5% and 10%, and 8 no significant rise. Older patients and very toxic patients gave the poorest response to this therapy. A much more rapid and effective return to normal can be obtained by transfusing fresh blood.

LABORATORY CONTROL

With the dosage of heparin described above, the clotting-time has been sufficiently prolonged to control thrombosis but not to cause hæmorrhage. Laboratory control with this dosage of heparin is therefore unnecessary.

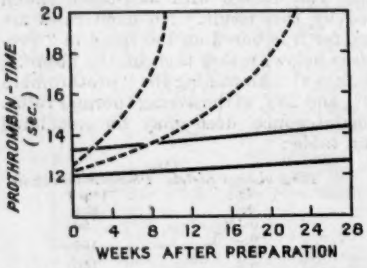

Fig. 3—Decay in potency of stored extracts of brain. Mean prothrombin-times of 10 normal plasmas: continuous line, freeze-dried extract of brain stored at room-temperature; interrupted line, acetone-dried extract of brain stored in desiccator at 4°C.

The use of anti-prothrombin agents must be subject to careful laboratory control. The depression of factor VII was estimated by a modification of the Quick one-stage method (Quick et al. 1935). The technique of the estimation is described by Ball and Hughes (1949). In the present study, however, a freeze-dried preparation has superseded the fresh saline extract of brain as thromboplastin. This method has the following advantages:

(1) Enough extract of brain for about six months' use can be prepared at one operation. This obviates differences in preparations made on consecutive days.

(2) Frequent estimations of the thromboplastin are not required.

(3) The preparation can be stored at room-temperature, special precautions of storage at 4°C or in vacuo being unnecessary.

(4) The product will remain potent longer (fig. 3).

(5) In view of the less frequent need of estimations, the ease of storage, and the length of active life of freeze-dried extract of brain, a batch can be prepared and estimated by a central laboratory, and supplies provided, with curves of their thromboplastin content, to the peripheral laboratories of the region. This has been done around Cambridge for more than a year with good results. By this means a larger number of patients can be treated.

(6) Since the estimations are more reliable and daily variations are reduced, patients can be treated in their own homes in the area around the pathological laboratory.

TABLE I—DISEASE IN 1135 TREATED CASES OF THROMBO-EMBOLISM

	No. of patients	
	Male	Female
After operation:		
Deep venous thrombosis (D.V.T.)	144	152
Superficial venous thrombosis	32	52
D.V.T. + pulm. embolism	18	14
Pulm. embolism without obvious D.V.T.	6	7
Pelvic-vein thrombosis	..	8
Medical cases:		
Deep venous thrombosis	62	69
Superficial venous thrombosis	94	136
D.V.T. + pulm. embolism	5	4
Pulm. embolism without obvious D.V.T.	9	4
Pelvic-vein thrombosis	..	1
Cerebral thrombosis	3	3
Retinal-vein thrombosis	..	4
Arterial embolism	4	1
After parturition:		
Deep venous thrombosis	..	81
Superficial venous thrombosis	..	206
D.V.T. + pulm. embolism	..	12
Pulm. embolism without obvious D.V.T.	..	3
Cavernous-sinus thrombosis	..	1

Of these patients 307 were treated at home.

Results and Discussion

During the past five years 1135 cases of peripheral venous thrombosis have been treated in the Cambridge area. A further 134 cases were treated for cardiac infarction without thrombosis in other parts of the body, but these have been excluded from the present series. The disease present in the remainder is shown in table I. It is convenient to consider the results of treatment under the headings of mortality and morbidity.

MORTALITY

Of the 1135 patients treated only 3 died. In table II the Cambridge figures are compared with those of Bauer (1946) and Ball and Hughes (1949), and it can be seen that our results compare favourably with those at other hospitals.

Two of the deaths in the present series were due to massive pulmonary embolism in patients in whom superficial venous thrombosis alone had been diagnosed in life. All 3 deaths are worthy of detailed record.

Case 1.—A man, aged 56, was seen for a local practitioner, and a very mild superficial venous thrombosis of the thigh was diagnosed. The thrombophlebitis, although only involving superficial veins, was spreading slowly, and anticoagulants were therefore given. The condition responded within three days, and the patient was discharged. Ten days later a fresh

TABLE II—CASE-MORTALITY IN TREATED THROMBO-EMBOLIC DISEASE

—	Case-mortality (%)			
	Without treatment (Bauer 1946)	Heparin (Bauer 1946)	Ball and Hughes (1949)	Cambridge
After surgical operations ..	16·6	1·4	1·3*	0·5
After parturition	3·6	..	0	0
Medical cases	19·0	..	..	0·2†

* 2 cases of pulmonary embolism before treatment.
† Including 1 patient who died after treatment was stopped.

attack developed in the same leg; this seemed to be extremely mild and superficial. The laboratory was not informed, nor were anticoagulants given. Two days later the patient died from a massive pulmonary embolus. Necropsy revealed a very extensive deep-vein thrombosis as well as the superficial one. This deep-vein thrombosis had presented no symptoms or signs in life.

Case 2.—A woman, aged 45, admitted for a gynæcological operation was found to have bilateral superficial venous thrombosis of the thigh. It was considered that the thrombosis might extend postoperatively; so anticoagulant therapy was instituted. After a few days, and before she could be operated on, her condition deteriorated, and she developed left-sided heart-failure and died. Necropsy revealed a massive pulmonary embolus. The clot appeared to be many days old and had probably formed before the patient's admission to hospital. The leg veins, both superficial and deep, showed extensive old and recent thrombosis. The deep-vein thrombosis had presented no symptoms or signs in life.

Case 3.—A man, aged 55, seven days after a total gastrectomy for carcinoma, having been up and walking for four days, had swelling and tenderness of the left calf. No pain, tenderness, or swelling was present in the right leg. Anticoagulant therapy was instituted. Three hours later the patient died. Necropsy revealed a massive pulmonary embolism which had

TABLE III—AVERAGE LENGTH OF STAY IN BED AND TIME TO DISAPPEARANCE OF PAIN IN TREATED CASES OF LEG-VEIN THROMBOSIS

—	Conservative treatment	Bauer (1946)	Cambridge
Time to freedom from pain:			
D.V.T. and pulm. emb. ..	About 35 days	4 days	3–4 days
S.V.T.	..	..	18 hours
Average stay in bed:			
D.V.T. and pulm. emb. ..	40 days	4–7 days	5–7 days
S.V.T.	..	..	3–5 days

come not from the left leg but from the right leg, which had shown no signs of thrombosis in life.

MORBIDITY

The morbidity can be considered under two headings: length of stay in hospital, and sequelæ.

Stay in hospital.—The length of stay in bed and the attainment of freedom from pain are shown in table III and are compared with Bauer's (1946) results and with conservative treatment. In the present series the stay in bed was reduced by about thirty-five days—a considerable saving for the patient and for a busy hospital with a long waiting-list.

Sequelæ.—No follow-up has yet been done to determine late sequelæ. Figures are available, however, of the number of cases in which there was swelling of the leg on discharge from hospital (table IV). A few of these cases seen later show hardly any swelling. Table V shows that nearly all these patients with residual swelling were not treated until several days after the development of pain in the leg. Prompt treatment is therefore important in reducing the incidence of undesirable sequelæ.

Value of Combining Heparin Therapy with Treatment by Anti-prothrombin Agents

At an early stage of the present study the standard treatment was with dicoumarol and heparin for the first thirty-six hours. The introduction of the rapidly acting ethyl biscoumacetate suggested that cover with heparin might be stopped.

Without heparin both the time spent in bed and, even more important, the duration of pain were lengthened. With heparin the relief of pain was often dramatic and rapid, but not with ethyl biscoumacetate. In view of these findings treatment with heparin was reinstituted. The results of each form of treatment are shown in table VI. These results show that, for maximal speed in relief of pain and for reducing the stay in bed to a minimum, heparin must be given for a few hours even when the rapidly acting ethyl biscoumacetate and phenylindanedione are used.

Patients treated at home cannot easily be given the full course of heparin, but in such cases a single initial intramuscular dose of 150 mg. of heparin may be of definite value.

TABLE IV—INCIDENCE OF SWELLING ON DISCHARGE FROM HOSPITAL IN PATIENTS TREATED FOR LEG-VEIN THROMBOSIS (PATIENTS TREATED AT HOME HAVE BEEN EXCLUDED)

Swelling	Medical cases	Surgical cases	Obstetric cases
Mild	41	39	20
Moderate	4	6	3
None	222	322	171

Domiciliary Anticoagulant Therapy

The use of freeze-dried extract of brain, which insures accurate prothrombin estimations, and the development of safer anti-prothrombin agents have made possible domiciliary anticoagulant therapy.

In the Cambridge area 307 patients have been treated in their own homes during the past four years. No unfortunate side-reactions have been observed.

The initial dose of the anti-prothrombin agent is given when the original diagnosis is made, together with an intravenous injection of heparin if possible. The patient is visited by the pathologist next day for estimation of the prothrombin level and thereafter as necessary to control the therapy. About four or five visits by the pathologist are usually sufficient to complete the treatment, and the results are almost as good and rapid as those of hospital therapy.

Although this form of therapy necessitates a few outside visits by the pathologist, the saving in hospital beds fully compensates for the inconvenience.

Pulmonary Embolism

The fatal pulmonary embolus has, to our disappointment, in the great majority of cases been unheralded.

Seventy deaths due to massive pulmonary embolism, confirmed by necropsy, have taken place in the hospital in the past seven years, during which time early ambulation and postoperative exercises have been encouraged in surgical wards. Since 1949 efforts have been made to diagnose deep-vein thrombosis of the leg in its earliest stage, and such cases have received immediate and adequate therapy with anticoagulants. It was hoped that this early diagnosis and treatment of thrombosis

TABLE V—INTERVAL BETWEEN ONSET OF THROMBOSIS AND START OF TREATMENT IN PATIENTS SHOWING SWELLING OF LEG ON DISCHARGE FROM HOSPITAL

Days after onset..	0–3	3–6	6–9	More than 9
No. of cases ..	6	22	70	15

TABLE VI—VALUE OF COMBINING HEPARIN THERAPY WITH TREATMENT BY ANTI-PROTHROMBIN AGENTS

Disease	Dicoumarol plus heparin for first 36 hr.			Ethyl biscoumacetate			Ethyl biscoumacetate plus heparin for first 18 hr.		
	No. of cases	Average time to freedom from pain	Average stay in bed	No. of cases	Average time to freedom from pain	Average stay in bed	No. of cases	Average time to freedom from pain	Average stay in bed
Deep vein thrombosis and pulmonary embolism	37	3 days	5·6 days	107	5 days	7·3 days	215	3 days	4·9 days
Superficial vein thrombosis	26	1 day	3·5 days	96	2 days	5·4 days	210	18 hours	2·6 days

would either eliminate or considerably reduce the mortality from massive pulmonary embolus.

In spite of the vigilance of residents, nurses, and physiotherapists, who were made fully aware of the significance of calf pain and tenderness, deaths from pulmonary emboli have continued to take place (table VII). It must be emphasised again that these fatalities (apart from 2 cases previously described) took place in patients who gave neither symptoms nor signs of leg-vein thrombosis and had therefore received no treatment with anticoagulants.

TABLE VII—TOTAL MORTALITY DUE TO THROMBO-EMBOLIC DISEASE

—	Surgical cases	Medical cases	Total
1947	4	5	9
1948	6	1	7
1949	6	4	10
1950	13	6	19
1951	8	..	8
1952	4	4	8
1953	8	1	9

Only cases of massive pulmonary embolism are included, all confirmed by necropsy and considered by the pathologist to be the main cause of death.
Anticoagulant therapy was begun in 1949.

Although some cases might have been diagnosed by the more careful search of an experienced clinician, signs of leg-vein thrombosis must have been minimal, or absent in most of them. There are three possible reasons for failure to diagnose this condition :

(1) In 12 cases (17%) the origin of the fatal embolus was found at necropsy to be at a site other than the veins of the calf (table VIII). (In 68 of the 70 necropsies the calf veins were examined for clot.)

(2) On examining the calf muscles in 2 recent cases at necropsy, it was noticed that thrombus filled only a few of the smaller calf veins in the bellies of the soleus muscles. Moreover these veins were clotted for only about 1 cm. from their junction with the posterior tibial vein, which contained ante-mortem clot. Neither patient had calf tenderness on examination before death. Case 3 (see above) illustrates well that a fatal embolus may come not from a painful leg but from a painless one.

As Murley (1950) suggests, the pain in the calf is probably due to distension of the intramuscular veins with clot. If this clotting is minimal before spreading to the trunk of the posterior tibial vein, such cases may possibly not show the severity of tenderness associated with more extensive clotting. This suggestion awaits confirmation by more detailed investigation on the post-mortem table and under the microscope.

(3) Dew (1953) has claimed that intravascular pulmonary thrombosis develops commonly as a primary lesion. Some of the "silent" cases in the present series may fall into this category. In many cases, however, the responsible embolus was coiled or doubled on itself in the pulmonary artery and appeared to have originated in a vessel smaller in calibre than the one in which it finally lodged.

Probably each of these conditions may account for a proportion of the "silent" pulmonary emboli.

Conclusions

On the basis of five years' use of anticoagulants the following conclusions may be drawn :

(1) The morbidity of both deep and superficial venous thrombosis can be considerably reduced by treatment.

(2) Combined treatment with heparin and an anti-prothrombin agent gives better results than does treatment with anti-prothrombins alone.

(3) Anticoagulant therapy has not materially influenced the incidence of massive fatal pulmonary embolism. The fatal pulmonary emboli are sudden and silent and usually produce no signs before death.

(4) In a busy hospital of 500 beds an average of 10 fatal pulmonary emboli will occur each year. Methods for preventing these deaths are being investigated.

(5) Many patients with thrombo-embolic diseases can be treated effectively and safely at home if laboratory coöperation can be obtained.

Summary

The Cambridge method of treatment with heparin and anti-prothrombin agents is described, and the results of treatment of 1135 cases of venous thrombosis are given. Only 3 deaths took place among the treated cases. The

TABLE VIII—ORIGINS OF FATAL EMBOLI FROM SITES OTHER THAN CALF

Case no.	Age (yr.)	Sex	Disease	Site of thrombosis	State of calf veins
4	67	F	Pernicious anæmia	Left renal vein	Calf veins not examined but no clot expressed from either femoral vein
5	68	M	Gastric ulcer, hæmatemesis	Right internal iliac vein	Free from clot (examined histologically)
6	47	F	Rheumatic fever	Adherent ante-mortem clot in right auricular appendix) (patent I-V septum)	Free from clot
7	23	F	"Phlebitis," pregnancy	Right long saphenous vein, extending into femoral vein	Free from clot
8	53	F	Carc. uteri, panhysterectomy	Left ovarian vein, extending to internal iliac vein	Free from clot
9	69	M	Heart-failure, fibrillation	Ante-mortem clot in right and left auricular appendages	Calf muscles not sectioned, but no clot in either femoral vein
10	77	F	Fractured femur	Veins thrombosed around site of fracture, extending into profunda vein and thence to femoral vein	Free from clot
11	54	F	Gastric ulcer, partial gastrectomy	Thrombosis of left subclavian vein	Free from clot
12	48	F	Fibroids, hysterectomy	(1) Vaginal branches of left internal iliac vein ; (2) right internal iliac vein	Free from clot
13	73	F	Appendicitis	Right profunda vein	Free from clot
14	49	F	Partial gastrectomy	In one branch of a double femoral vein on left side	Free from clot
15	73	M	Bronchitis	Right profunda vein	Free from clot

incidence of fatal pulmonary emboli was not reduced by anticoagulant therapy. Failure to diagnose the presence of thrombosis is discussed.

The length of stay in hospital was reduced by an average of thirty-five days. 13·6% of the patients had swelling of the legs on discharge from hospital (12·4% mild, 1·2% moderate); prompt treatment is important in avoiding this sequela.

Combination of heparin and anti-prothrombin agents is important to shorten the stay in bed and to relieve pain quickly.

Domiciliary anticoagulant therapy has been rendered safe by the use of freeze-dried extract of brain for prothrombin estimations and by the development of safer anticoagulants. 307 of the patients in this series were treated successfully at home.

Conclusions are drawn from our experience in the use of anticoagulants during the last five years.

We wish to thank the consultant physicians and surgeons of the United Cambridge Hospitals, and the general practitioners of the Cambridge area, for permission to publish. The investigations on the fatal pulmonary emboli would not have been possible except for the careful necropsy examinations done by Dr. A. M. Barrett, whom we wish to thank. Roche Products provided the vitamin K_1.

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DISSECTING AORTIC ANEURYSM IN *MARFAN'S SYNDROME*

S. R. F. WHITTAKER
M.A., M.D. Camb., F.R.C.P.
PHYSICIAN, SOUTH WARWICKSHIRE GROUP OF HOSPITALS

J. D. SHEEHAN
M.D. N.U.I., M.R.C.P.
SENIOR REGISTRAR, NOTTINGHAM AND DISTRICT CHEST CENTRE

SINCE Marfan (1896) first described the multiple skeletal defects which were grouped later under the title "arachnodactyly," many other manifestations of the syndrome have been reported.

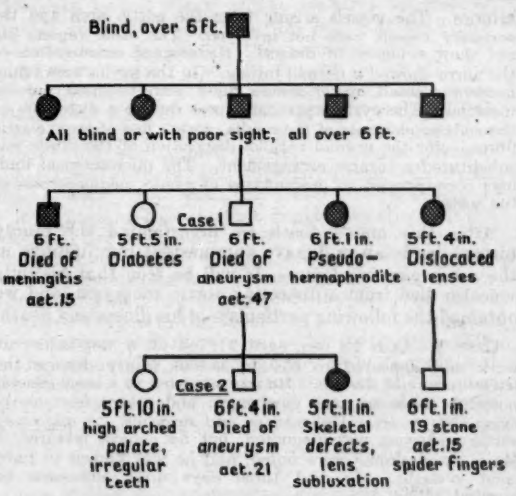
Important landmarks in the descriptive literature are:

(1) *Skeletal abnormalities:* abnormal height with long slender extremities and spider-like fingers and toes (Marfan 1896); high arched palate (Boerger 1915); and double row of teeth (Bauer 1927).

(2) *Ocular abnormalities:* shallow anterior chambers (Salle 1912) and congenital dislocation of the lens (Boerger 1915). Probably about 60% of the cases showing other features have ocular abnormalities (Rados 1942).

(3) *Cardiovascular abnormalities:* patent foramen ovale (Salle 1912); mitral and aortic valvular disease (Ormond 1930); aneurysmal dilatation of the aortic arch (Baer et al. 1943); dissecting aortic aneurysm (Etter and Glover 1943); and "myocarditis" (Whitfield et al. 1951).

The cardiovascular lesions associated with arachnodactyly are well reviewed by Reynolds (1950) and Marvel and Genovese (1951). Thomas et al. (1952) consider that fusiform aneurysms of the aorta due to cystic medionecrosis represent the most serious complication in Marfan's syndrome, and that dissection of the aorta is often the cause of early death.


Blind, over 6 ft.
All blind or with poor sight, all over 6 ft.
6 ft. Died of meningitis aet. 15
5 ft. 5 in. Diabetes
Case 1
6 ft. Died of aneurysm aet. 47
6 ft. 1 in. Pseudo-hermaphrodite
5 ft. 4 in. Dislocated lenses
Case 2
5 ft. 10 in. high arched palate, irregular teeth
6 ft. 4 in. Died of aneurysm aet. 21
5 ft. 11 in. Skeletal defects, lens subluxation
6 ft. 1 in. 19 stone aet. 15 spider fingers

Patient's family tree: hatched, ocular defects.

Goyette and Palmer (1953) emphasise that in young persons with arachnodactyly the heart is often considered normal, but nevertheless in adult life classical signs of aortic insufficiency can be detected in some cases, and death from either heart-failure or dissection of an aneurysm is common.

(4) *Hereditary and familial tendencies* were first mentioned by Achard (1902), but Rados (1942), who reviewed the published cases, found a family history in less than 40%. Until recent years, however, this aspect of the syndrome has received less attention than it deserves.

We report here two cases of dissecting aortic aneurysm occurring as an isolated lesion in members of a family showing other features of Marfan's syndrome (see figure).

Case-reports

Case 1.—A man, aged 46, attended the outpatient department at Stratford-on-Avon Hospital on March 9, 1950, complaining of 12 months' dyspnœa on exertion. His heart was enlarged, and he had a loud to-and-fro murmur at the aortic area. His blood-pressure was 160/30 mm. Hg. Radiography revealed a large left ventricle with fusiform dilatation of the thoracic aorta, especially of its ascending part. There was no radiological evidence of mitral-valve disease, and the lung fields were normal. There was no antecedent history of rheumatic infection, and Wassermann and Kahn reactions were negative. The cause of the aneurysm remained in doubt because no other features of Marfan's syndrome were evident. The patient was lost sight of for eighteen months, but during that time angina of effort was a prominent symptom. On Oct. 2, 1951, his chest pain became severe and unrelenting and was not relieved by glycerol trinitrate. Next day he developed pain in the lower back and suppression of urine. On admission to hospital that evening he had lost the use of his legs, which were extremely painful.

On examination the arteries of his neck and arms were pulsating violently, but no pulse could be felt in the femoral vessels. The cardiac apex-beat was found in the sixth interspace in the left anterior axillary line and was forcible. The blood-pressure was 250/0 mm. Hg, and the cardiac murmurs were unchanged. There was complete flaccid paralysis of both legs. A dissecting aortic aneurysm was diagnosed, and death took place twelve hours after admission to hospital.

Necropsy showed no external evidence of disease in a man who, although 6 ft. tall, was of average build. The heart was much enlarged, with an enormously hypertrophied left ventricle. The aortic valve was dilated and incompetent but without disease of the valve cusps. No mitral valvular disease was found. In the first part of the ascending aorta there was a large aneurysmal dilatation. Dissection of the aneurysm had taken place, extending into the common iliac

arteries. The vessels arising from the aortic arch and the coronary vessels were not involved. The other organs did not show evidence of disease. Histological examination of the aorta showed a normal intima. In the media were found numerous small cystic spaces filled with basophil mucoid material. The cystic appearance was due to a distortion of the cellular elements of the media, with a loss of large elastic fibres. For the normal parallel disposition of the fibres was substituted a bizarre arrangement. The microscopical findings corresponded to descriptions of cystic medionecrosis of the aorta.

After this man's death we investigated the family history in detail and have summarised our findings in the accompanying figure. It will be seen that his only son also died from a dissecting aortic aneurysm, and we obtained the following particulars of his illness and death.

Case 2.—Case 1's son, aged 21, fell off a step-ladder at work and appeared to sustain serious injury despite the trivial nature of the fall. He was admitted to a large general hospital as a surgical emergency and was subsequently examined by several physicians and surgeons. A dissecting aortic aneurysm was diagnosed, but no clinical features of Marfan's syndrome were noted, and he was known to have good eyesight. He died three days after admission to hospital.

Necropsy showed the body of a tall well-built male with no external evidence of arachnodactyly or any other disease. The pericardial cavity was distended with fresh blood-clot. The aortic valve was dilated and the left ventricle hypertrophied. The mitral valve appeared normal. The first portion of the aorta had an irregular tear in the intimal surface, with a dissecting aneurysm extending inferiorly to surround the right side of the aortic valve and to encircle the right coronary artery. The aneurysm communicated with the pericardial cavity. There was no extension into carotid or subclavian vessels, but the whole of the thoracic and abdominal aorta was involved as far as the bifurcation. The liver, spleen, and kidneys were of normal size and on section revealed only acute engorgement with blood. The other organs appeared normal. The pathologist reported medial degeneration of the aorta as the cause of the aneurysm.

Discussion

The interest in these two cases of dissecting aortic aneurysm lies in the absence of other defects described for Marfan's syndrome, although a strong family history of the condition exists (see figure). Dissecting aneurysm of the aorta is not rare, and Schnitker and Bayer (1944) found 25% of 580 such aneurysms in persons aged less than 40; they believed aortic medionecrosis to be the commonest cause of the aneurysm. From our experience of the two present cases it seems that some cases of dissecting aneurysm may be unrecognised examples of Marfan's syndrome. For this reason we suggest that in all cases of dissecting aneurysm or unexplained aortic dilatation careful search be made into the family history and for other manifestations of the syndrome. The retention of the eponym "Marfan's syndrome" rather than "arachnodactyly" may be a reminder that visceral lesions without obvious skeletal or ocular defects may be the sole evidence of the anomaly.

Summary

The chief features of Marfan's syndrome are briefly reviewed.

Two cases of dissecting aortic aneurysm (due to medionecrosis) without other evidence of the syndrome are reported in a family showing many affected members.

In cases of dissecting aneurysm search for other congenital anomalies and for familial disease should be made.

A plea is made for retention of the title "Marfan's syndrome" rather than "arachnodactyly."

Our thanks are due to Dr. D. F. Barrowcliff and Dr. R. L. Bishton for the necropsy reports.

References at foot of next column

AN UNUSUAL CASE OF DISSECTING ANEURYSM OF THE AORTA

W. BRUMFITT
M.B. Lond., M.R.C.P.
FORMERLY RESIDENT CLINICAL PATHOLOGIST, GLOUCESTERSHIRE ROYAL HOSPITALS

N. E. RANKIN
M.B. Lond.
ASSISTANT PATHOLOGIST, HOPE HOSPITAL, SALFORD; FORMERLY ASSISTANT PATHOLOGIST, GLOUCESTERSHIRE ROYAL HOSPITALS

DISSECTING aneurysm of the aorta, although it often produces a clear-cut clinical picture, may occasionally produce symptoms which are confused with those of myocardial infarction. The following case demonstrates the disastrous results which followed anticoagulant therapy.

Case-report

A farm-worker, aged 42, was admitted to the City General Hospital, Gloucester, complaining of severe pain in the chest.

Previous History.—In 1935 he applied for a job but was turned down because of high blood-pressure. In 1936 he had a "nervous breakdown" because of worry about his blood-pressure and was off work for a year. There was no history of renal disease.

Family History.—His father died at the age of 52 after a stroke.

Present History.—After an argument the patient had a severe pain in the centre of his chest. He vomited twice and was given 'Omnopon' gr. $^1/_3$ by his doctor before being sent to hospital. The pain was still severe on admission, and he also complained of discomfort in the right loin. The chest pain did not radiate into the neck or into either arm.

On examination he was well built but rather obese. He was dyspnœic, propped up in bed, and appeared anxious. His pulse-rate was 64 and blood-pressure 240/140 mm. Hg in both arms. The femoral pulses were present and equal. The apex-beat of the heart was heaving and in the 6th left intercostal space in the anterior axillary line. No pericardial rub was heard. The heart sounds were heard in all precordial areas, and at the base the second aortic sound was accentuated. A blood-count showed leucocytosis.

Treatment and Course.—Myocardial infarction was diagnosed and anticoagulant therapy started (heparin 12,500 units intravenously four-hourly and ethyl biscoumacetate 1200 mg. orally). Two hours after the first dose of heparin the pain in the right loin became severe, and soon afterwards a sudden and severe bursting pain came on in the chest, just under the sternum. The patient was pale and sweating, and the blood-pressure in his right arm was 70/50 mm. Hg, although the heart sounds were still clearly audible. An hour later he complained of numbness in the right leg, and the femoral pulse on this side was now much weaker than on the left. He became progressively weaker and died next morning.

Investigations.—Electrocardiography five hours after the exhibition of anticoagulants showed left ventricular stress, suggesting a high lateral infarct (fig. 1). The blood-urea level was 45 mg. per 100 ml. Wassermann and Kahn tests were negative. Hæmoglobin 105% (15·2 g. per 100 ml.). White cells 15,900 per c.mm. (polymorphs 14,628, lymphocytes 1113,

DR. WHITTAKER, DR. SHEEHAN: REFERENCES

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mononuclears 159 per c.mm.). Erythrocyte-sedimentation rate 2 mm. in 1st hr. (Wintrobe). Routine chemical analysis of the urine showed no abnormality.

Necropsy Findings.—The body was that of a middle-aged man. The heart showed considerable left ventricular hypertrophy. The muscle appeared healthy, and the valves were normal. The coronary arteries were patent. There was a large dissecting aneurysm of the aorta splitting the media throughout its length (fig. 2). There was extravasation of blood round the origin of the left coronary artery, into the neck round the carotid arteries, along the subclavian arteries, and into the posterior mediastinum. There was a very large hæmorrhage into the retroperitoneal tissues, extending into the splenic ligament, along the greater curvature of the stomach, the mesentery, and mesocolon, and laterally round both kidneys, especially on the right side. Inferiorly it extended along both common iliac arteries. The left kidney was hydronephrotic and represented by a thin-walled sac. Histologically some small areas of functioning kidney tissue were identified; the remainder consisted of fibrous tissue with atrophic tubules filled with "colloid" material. The left renal artery was small and atrophic. The right kidney was greatly hypertrophied but normal macroscopically. Microscopically the glomeruli and tubules were large, showing compensatory hypertrophy. A few glomeruli showed early hyaline change, and a few arterioles showed some changes of benign hypertension. The stomach and intestines were distended and contained some changed blood. The lungs were œdematous.

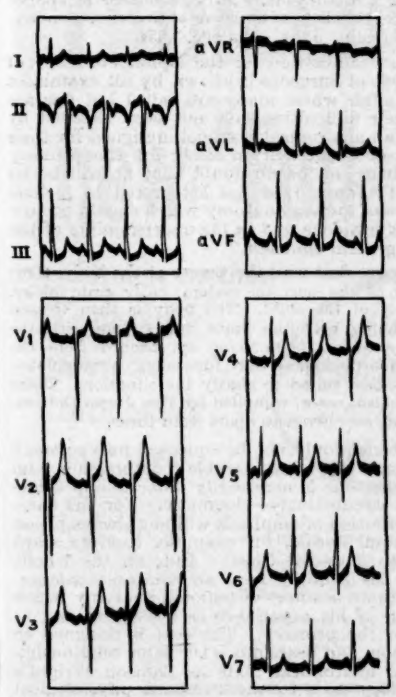

Fig. 1—Electrocardiogram showing left ventricular stress suggesting a high lateral infarct.

Discussion

Several important points are illustrated by this case, the difficulties arising in the diagnosis of myocardial infarct and the possible danger of anticoagulants. The importance of investigating hypertension fully when it occurs in young adults is re-emphasised. The error arose because of the confusion of the presenting symptoms with those of myocardial infarction: the crushing pain in the chest which persisted, vomiting, pallor, and sweating. Later, leucocytosis appeared to confirm the diagnosis. It was not until severe pain developed in the loin and then numbness of the leg that the true diagnosis was established.

Dissecting aneurysm might have been suspected because of certain symptoms and signs which were not typical of myocardial infarction: (1) the nature of the pain, which was agonising from the start and situated deeply in the chest; (2) the presence of initial pain in the right loin; and (3) the nature of the heart sounds—the apical first sound remained clear and loud.

This case lacked many of the classical features of dissecting aneurysm: the pain did not shift until late or radiate into the back; the blood-pressure in the two arms was equal; and the femoral pulses did not seem to differ. Myocardial ischæmia may have been present at the time of electrocardiography and was due to the fact that the dissecting aneurysm involved the orifice of the left coronary artery. Similar electrocardiographic changes are not uncommon (MacCuish 1953). It is not clear when this vessel became involved, but it is certain that further rapid dissection of the aortic wall followed soon after the administration of anticoagulants. This would account for the very extensive hæmorrhage found in this case.

The leucocytosis can be explained by the presence of extravasated blood in the tissue.

Hypertension was discovered in the patient in 1935, when he was only 27, and was probably due to unilateral renal disease. It seems unfortunate that the kidneys were not investigated at that time, because good results might have followed the removal of the diseased kidney.

Summary

A case of dissecting aneurysm of the aorta is described. The symptoms closely simulated those of myocardial infarction, and anticoagulant therapy was started. The necropsy findings are described, and the difficulties of diagnosis discussed.

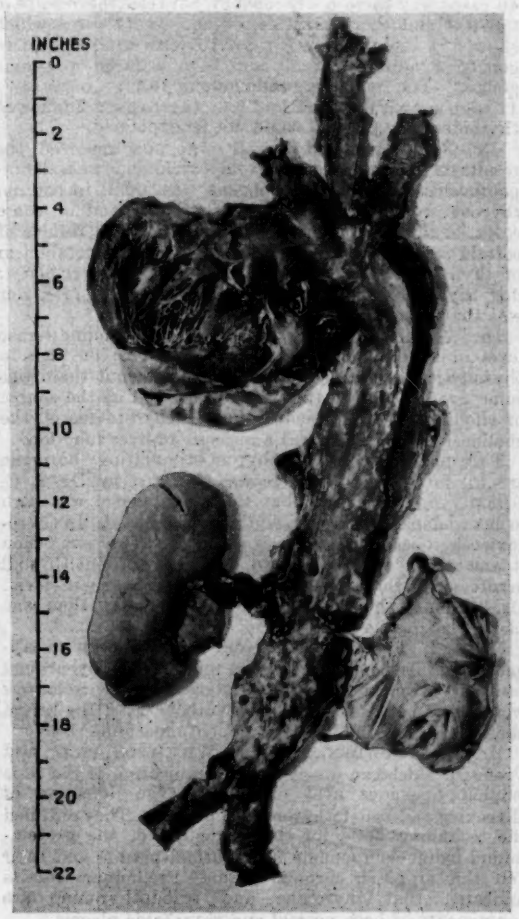

Fig. 2—Necropsy specimen of heart, aorta, and kidneys.

We wish to thank Dr. R. F. Jarrett and Dr. E. N. Davey for permission to publish; Miss M. Collins for the electrocardiogram; and Mr. H. Walwin for the photograph of the pathological specimen.

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Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS AND ASSOCIATION OF CLINICAL BIOCHEMISTS

Thyroid Function

DURING a joint meeting of the two associations at Brighton on Oct. 2 one session was devoted to thyroid *function*.

Prof. E. J. WAYNE discussed the use of radio-iodide in the diagnosis of thyroid disorders. It was preferable to use two or three tests, especially the determination of the thyroid uptake of radio-iodide four hours after a dose and the plasma protein-bound activity forty-eight hours after a dose. The latter corresponded most closely to the final clinical diagnosis in hyperthyroidism; on the other hand, tests based on urinary excretion were specially valuable in the diagnosis of hypothyroid states.

The results of some 500 cases in which the I^{131} thigh-neck clearance test was used were reviewed by Dr. B. W. MEADE and Prof. N. F. MACLAGAN. In only 40 cases was there a discrepancy between the results of the test and the clinical condition. In 17 cases which showed a high clearance rate, 16 were attributable to goitrogen administration and 1 to a large non-toxic goitre. The remaining anomalous results were low: 11 were caused by iodide and 6 by thyroxine; 2 followed thyroidectomy; and 4 could not be explained.

Dr. F. BROWN and Dr. H. JACKSON reported the results of treatment of thyroid carcinoma with therapeutic doses of I^{131}. The plasma was found to contain thyroid protein in addition to thyroxine and in some cases small amounts of diiodotyrosine. The results of certain animal experiments showed that the metabolism of thyroid protein shows a definite species specificity: dog thyroid protein was not metabolised by rats, nor was that from rats metabolised by dogs.

Dr. A. TICKNER discussed the serum cholinesterase level in thyroid disease. It was found to be high in thyrotoxic states and low in myxœdema, but there was some overlap. Since the liver is regarded as the source of cholinesterase, it seemed that in thyrotoxicosis, the cholinesterase activity was a measure of liver function.

The measurement of thyroid-stimulating hormone (T.S.H.) in thyroid disorders was reported by Dr. I. C. GILLILAND. He found that the plasma level was high in myxœdema and low in Simmonds's disease. In thyrotoxicosis it was low unless eye signs were present, when it was raised. In cases of exophthalmos without thyroid involvement there was no increase in the T.S.H. level. Dr. Gilliland therefore concluded that more than one factor was involved.

Mr. A. L. TÁRNOKY, PH.D. and Dr. P. WHITE investigated the relationship between a number of conventional tests in thyroid disease. Highly significant correlations were found between the basal metabolic rate, the serum cholesterol, and the urinary pigment/creatinine ratio.

Mr. C. H. BOWDEN, Mr. J. H. WILKINSON, PH.D., and Professor Maclagan described the application of the ce ic sulphate-arsenious acid reaction to the detection of thyroxine and triiodothyronine in plasma. They outlined the techniques used for the extraction of the protein-bound iodine components from normal plasma and their detection on paper chromatograms. Preliminary results indicated that thyroxine and triiodothyronine are components of both normal and thyrotoxic plasma.

Reviews of Books

Anatomy, Regional and Applied

R. J. LAST, M.B. Adelaide, F.R.C.S., professor of applied anatomy, Royal College of Surgeons of England. London: J. & A. Churchill. 1954. Pp. 665. 55*s*.

THE primary examination for the diploma of fellow of the Royal College of Surgeons is known by all examinees as a fearsome affair where many are called but few are chosen, and their difficulties have not been lessened by the absence of an anatomical textbook designed for their needs. This book is not written solely for the primary student, but there can be no doubt that he will be its best patron. Professor Last has attempted to include "all those parts of human anatomy which should occupy a place in the knowledge *and in the understanding* of the *student or the general clinician.*"

The first 63 pages deal with the tissues of the body, some general features of the nervous system, early embryology, and the anatomy of the child. The body is then treated regionally, beginning with the limbs and ending with the brain, the topographical facts being approached from the embryological, morphological, or functional standpoint—whichever seems best suited to clarify the situation. There are some biographical notes, compiled by Miss Jessie Dobson, of the college, but no references apart from these.

So much material could not be squeezed into so small a space without very considerable compression and selection, and the tone is necessarily didactic and sometimes—perhaps comfortingly—dogmatic. For the same reason the distribution of emphasis will not always please everyone: femoral hernia, for example, receives scant courtesy, and so does the tonsil. But, on the whole, Professor Last has skilfully kept an equitable balance, and he has given an account of regional anatomy which bears the stamp of his experience as a surgeon and as an examiner for the primary. The text is designed to be read as revision, and bears much the same relationship to the standard anatomical texts as Samson Wright's *Applied Physiology* does to the standard physiological ones.

In this beautifully produced book there are numerous clear illustrations, many of which have been drawn by the author. Throughout there is much evidence of Professor Last's skill as a teacher, and his book will lighten the burden of those for whom the revision of anatomy is an unwelcome but essential task.

B.C.G. and Vole Vaccination

A Practical Handbook. K. NEVILLE IRVINE, M.A., D.M. Oxfd, adviser in B.C.G. vaccination to the Oxford regional hospital board. London: N.A.P.T. 1954. Pp. 96. 12*s*. 6*d*.

THIS small handbook of B.C.G. vaccination is splendid: it presents the essentials clearly without being unnecessarily dogmatic, and it is well illustrated. Let us hope that its price will not prevent it from being as widely read as it deserves.

An Introduction to Physical Methods of Treatment in Psychiatry (3rd ed. London: E. & S. Livingstone. 1954. Pp. 351. 20*s*.).—Dr. William Sargant and Dr. Eliot Slater, in the preface to their third edition, admit they have set themselves a bewildering task: "the mere trickle of literature on the subject has now become a torrent." They are both strong swimmers, however, and the torrent has not overwhelmed them. They do not attempt to write a critical review of published work, but stick to their original intent on of sorting out limitations of newer and older methods, discussing indications and contra-indications, and describing techniques. The book, of course, has been extensively revised, and in particular the chapter on prefrontal leucotomy has been very fully and carefully rewritten. Alcoholic addiction now has a short chapter to itself. The well-being of the patient is much in the forefront of their assessment of methods; as they say in their preface, theory at present is inadequately developed, and it is more than ever necessary to remain close to the bedside, so as to judge from personal observation which new methods fill a gap and which are mere alternatives to older ones.

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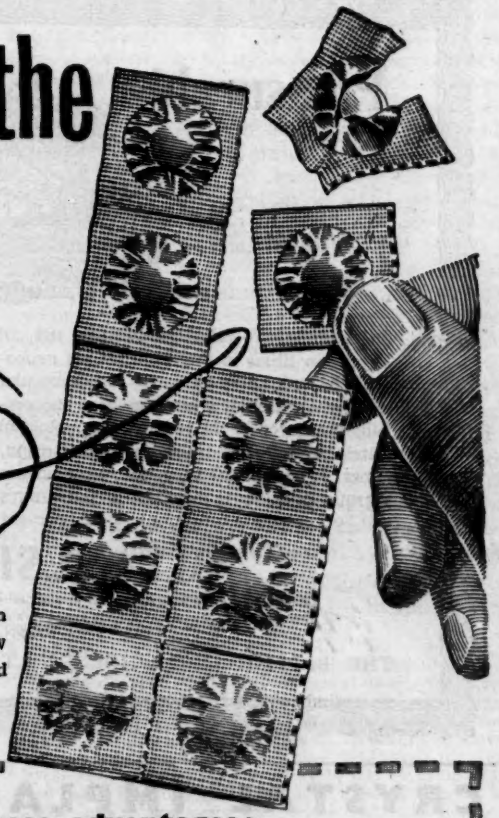

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THE LANCET
LONDON : SATURDAY, OCT. 16, 1954

Some Origins of Mental Symptoms

THE brain cells, like directors of a large concern, expect the best of everything: nourishing food, comfortable transport, an even temperature, a plentiful supply of oxygen, and perfect service all round the clock. Sometimes the service breaks down: their food may lack some essential constituent or contain others which are distasteful; or their cushioned ease may be shattered by collisions; or the temperature may become inconveniently high, or the oxygen supply inconveniently low. Whatever the affront, the neurones take it badly, becoming erratic in their work; and their aberrations are reflected in aberrant behaviour of the concern which they direct. Examples of two such affronts have lately appeared in our columns. Some weeks ago Dr. SHEILA SHERLOCK and others [1] described mental symptoms caused by a metabolic disturbance of the neurones, which had resented the presence in their blood-supply of substances less objectionable to other body cells; and in this issue, Dr. WILLIAM HUGHES and his colleagues describe mental symptoms caused by vascular changes in the region of the basal ganglia.

HUGHES et al. review 51 such cases, 15 of which they were able to study post mortem. They found distinctive lesions, and suggest that such cases form a recognisable, though not so far recognised, group.

All 51 patients had chronic arterial hypertension, with systolic pressures ranging from 140 to nearly 300 mm. Hg. and diastolic pressures ranging from 96 to 160 mm. Hg; all showed personality changes, emotional lability, and some degree of pseudobulbar palsy. Many of them had been hypertensive for a long time—one for at least eighteen years—but fluctuations in the blood-pressure could not be correlated with fluctuation in symptoms. After any acute episode (such as a stroke) the symptoms usually improved whether the blood-pressure rose or fell. Their emotional lability usually took the form of laughing or crying, but might manifest itself in outbursts of rage, very trying to relatives in the home or to other patients in the ward. The symptoms of pseudobulbar palsy included dysarthria, dysphagia (sometimes severe enough to reduce nutrition), and difficulty in phonation which seemed to come from an inability to use expiration in voice production. Some patients acquired the facial immobility, unblinking stare, and *marche à petits pas* which we associate with parkinsonism. In the early stages vertigo might be an incapacitating symptom, and there was evidence of numerous pyramidal and extrapyramidal lesions. The fundi showed arteriosclerotic changes.

1. Sherlock, S., Summerskill, W. H. J., White, L. P., Phear, E. A. *Lancet*, Sept. 4, 1954, p. 453.

The personality changes were striking. The patients became "out of sympathy" with their environment, caring nothing for the effect their behaviour might have on others. In many cases their excretory habits became offensive at a stage when they still gave the impression that they could control themselves if they liked. The effect of the dysphagia was to make some objectionable in their feeding habits: they wolfed their food like wild beasts. They declined into dementia, but the condition is so chronic that in some this took twenty years. Meanwhile their personality changes had alienated their friends and relations. The brains of the 15 cases examined post mortem contained multiple small lesions, showing various degrees of organisation of areas of ischæmic softening, in the region of the caudate nuclei and the anterior parts of the putamina; about two-thirds had scattered lesions in the thalamus. Midbrain, pons, medulla, and cerebellum showed few lesions, and the cortex was usually unaffected. Though the lesions were clearly ischæmic there was no evidence that the vessels had ever been totally occluded. HUGHES et al. do not feel that vascular spasm alone would account for the lesions, and they invoke an ingenious explanation in terms of hydrodynamics.

The 18 cases of cerebral disturbance in patients with liver disease, described by SHERLOCK et al., also had a vascular aspect.

In these patients, mental symptoms included clouding of consciousness, with confusion and apathy, progressing in some to coma. Emotional lability was common; facial expression was blank but not immobile, for the patients might grimace or blink. Speech was slow and slurred, and gradually became irrational in content. Symptoms might vary from day to day or hour to hour; and signs included a "flapping" type of tremor, which could affect not only the limbs but the neck, jaws, tongue, and eyelids. The gait was ataxic.

"Objective signs," these observers say, "indicate major involvement of the basal ganglia (which are particularly prone to toxic influences), the frontal cortex, and pyramidal systems; but critical appraisal suggests a diffuse cerebral disturbance." Three clinical factors combined, in varying degrees, to produce these disorders: serious liver disease, extensive portal-systemic venous collaterals, and a rise in nitrogenous substances in the blood. SHERLOCK et al. found that the neurological signs could be precipitated or enhanced either by giving ammonium chloride or methionine, or by increasing dietary protein above 60 g. daily. The evidence suggests that nitrogenous substances which normally pass through the liver and become metabolised were reaching the general circulation unchanged and proving toxic to the cerebral neurones. Blood in the portal vein is normally rich in nitrogenous material derived from the intestine; in the hepatic veins the level is much lower. But if the portal blood is by-passing the liver (because the portal vein is thrombosed or occluded), or if the damaged liver cannot metabolise these nitrogenous substances, they are liable to appear in the general circulation in much higher concentrations than usual; and, in fact, in these patients such was the case. The study was completed by withdrawing a large part of the nitrogenous content of the diet, when the mental symptoms remitted. Several patients, indeed, were restored to and maintained in good

mental health by diets containing less than 20 g. of protein.

These findings, of course, have an important practical application. High-protein diets, casein hydrolysates, amino-acid supplements, and ammonium chloride have had moderate success in the treatment of some forms of liver disease, and are widely used. It is as well to realise, as SHERLOCK and her colleagues point out, that they have potential dangers which are quite clear-cut; and that the patient who develops mental symptoms while being treated along these lines can be restored to reason by a reversal of the method of therapy.

But these two diverse groups of cases bring home a more general message. The well-being of the cerebral neurones can be disturbed by gross and permanent factors, such as deprivation of blood, or by subtle and temporary factors, such as changes—even perhaps minute changes—in the blood chemistry. The patient to whom they belong, however, has only a limited number of ways in which he can express their disorder: his repertoire of mental symptoms is relatively small, and cannot be a precise guide to the cause of his trouble. The tendency to classify mental diseases according to the bizarre behaviour or delusional ideas of patients has been very strong in the past and may well have hindered the growth of our understanding of mental disease. Studies such as the two discussed here help us to think more imaginatively of what is going on behind the façade of confusion, tears and laughter, anger, apathy, offensive habits, suspicion, self-blame, or whatever else cuts off the mentally ill person from his fellows.

Water Diuresis

IN this age of increasing organisation and diminishing returns in pure physiological research, not many could claim to have established the stimulus and mediation of a basic physiological response, either by themselves or with the help of a few others. Such a claim could, it seems, be fairly made by Prof. E. B. VERNEY, F.R.S. The evidence is contained in a John Malet Purser lecture which he delivered in Dublin earlier this year.[1]

The story begins in 1922, when STARLING and VERNEY observed that the isolated perfused dog kidney secreted a profuse and watery urine, and that this diuresis could be inhibited by adding posterior-pituitary extract to the perfusing blood.[2] The suggestion was made at that time that some substance with an action similar to that of posterior-pituitary extract was normally present in the intact animal. VERNEY has now traced "the experimental enquiry that has since been made into the events that underlie the ostensibly simple phenomenon of water diuresis." Circumstantial evidence on the type of mechanism involved was obtained from experiments showing that there was a lag of fifteen minutes between the maximum water-load and the maximum diuresis[3]; and that emotional stimuli inhibited the diuretic response to a water-load, this emotional inhibition not being significantly affected by renal denervation.[4] These observations suggested that the diuretic response to a water-load involved both a neural and a hormonal stage in transmission; but the precise nature of the stimulus initiating the chain of response could not directly be deduced. The most critical group of experiments in this regard was reported in 1947.[5] In dogs it was found that injection of hypertonic solutions of sodium chloride and sodium sulphate into the exposed carotid artery promptly inhibited water diuresis. Dextrose solutions of the same tonicity were not quite so effective as the sodium salts; and hypertonic urea did not inhibit the diuresis at all. It was concluded that the effective stimulus to the production of antidiuretic hormone (A.D.H.) was an increase in the osmolarity of the blood perfusing the carotid artery; the relevant osmotically active substances were, like sodium salts, limited in their capacity to enter cells and were not, like urea, free to enter them. Search for an end-organ likely to be sensitive to osmotic pressure of the surrounding fluid revealed in the supra-optic nuclei vacuoles, which were tentatively termed "osmoceptors"; these were thought to be the site of origin of a response, triggered off by a rise in ambient osmotic pressure, transmitted neurally to the posterior pituitary, and thence by the intermediation of A.D.H. to the renal tubule cells. Further work has filled in some of the details of the picture so convincingly outlined in 1947. It is now known that diuresis is inhibited by infusion over longer periods of solutions whose hypertonicity lies "within a range that may reasonably be regarded as physiological."[1] Further studies with ligation of branches of the internal carotid artery have narrowed the search for the receptors to the hypothalamus; and the posterior lobe itself has been excluded as a possible site.[6] The supra-optic vacuoles have been found to lie within cells of the nuclear clump of neurons.[7]

Increase in the effective osmotic pressure of plasma seems to be well established as a stimulus to A.D.H. output. VERNEY considers the difficulty arising from the observations that men on a low-salt diet do not remain in a state of water diuresis, while on the other hand water diuresis can be elicited in people retaining considerable amounts of previously ingested salt.[8] He suggests that under these circumstances change in A.D.H. activity is masked by change in the filtered load of salt and water. This explanation is not entirely satisfactory; for water diuresis may be lacking after very moderate salt deprivation, without detectable change in glomerular filtration-rate; and in Addison's disease and hypopituitarism the failure of water diuresis persists after adequate treatment with salt and deoxycortone acetate, but can be corrected by cortisone. Possibly the A.D.H. mechanism is the basis of a "short-term response" to acute changes in the osmolarity of body-fluid, but the volume (as opposed to the concentration) of body-fluid is regulated by mechanisms acting primarily on the excretion of sodium rather than of water, and mediated by adrenocortical hormones.[9] No single mechanism can be expected to explain everything; and it is the measure

1. Verney, E. B. *Irish J. med. Sci.* 1954, p. 377.
2. Verney, E. B., Starling, E. H. *J. Physiol.* 1922, **56**, 353.
3. Kisiecki, A., Pickford, M., Rothschild, P., Verney, E. B. *Proc. roy. Soc.* B. 1933, **112**, 496.
4. Rydin, H., Verney, E. B. *Quart. J. exp. Physiol.* 1938, **27**, 343.
5. Verney, E. B. *Proc. roy. Soc.* B. 1947, **135**, 25.
6. Jewell, P. A., Verney, E. B. *J. Endocrin.* 1952, **9**, p. ii.
7. Jewell, P. A. *J. Physiol.* 1953, **121**, 167.
8. Baldes, E. J., Smirk, F. H. *Ibid*, 1934, **82**, 62.
9. Black, D. A. K. *In* The Kidney. London, 1954.

of VERNEY's achievement that we know so much more about the control of water excretion than we do of the excretion of electrolytes. The discovery of electrocortin (aldosterone) has at last supplied a hormone of potency comparable to that of A.D.H.; but the mechanisms which stimulate or inhibit production of electrocortin have still to be defined.

Tuberculous Meningitis

THE therapeutic campaign against tuberculous meningitis is seven years old, and two recent reports show how substantial a victory has been won. LORBER [1 2] of Sheffield and TAYLOR [3] of Oxford agree that the lives of three-quarters of all patients, and more than 90% of those who are conscious on admission, can now be saved. LORBER's material was pædiatric, whereas TAYLOR's was "ephebiatric"[4]; and the agreement between their main conclusions is therefore the more striking. They confirm that early diagnosis is the first essential, and that the patient's mental state is the best guide to prognosis. Streptomycin is still the main prop of treatment, and intrathecal administration is still necessary. Ancillary chemotherapy is required, and for this purpose isoniazid has replaced *p*-aminosalicylic acid. Intrathecal tuberculin sometimes brings about dramatic improvement. Deafness is the commonest serious residual lesion, and permanent damage to the central nervous system is not rare.

Three important problems are now being attacked: deafness due to streptomycin; the mortality in grade-3 (most severely affected) cases; and permanent lesions in the central nervous system. In Oxford and in Sheffield both the dosage and duration of streptomycin treatment are being cautiously scaled down; and the incidence of deafness is falling. The mortality-rate in grade-3 patients and the incidence of neurological sequelæ are related problems. Cerebral lesions have in the past received most attention; but BROOKS et al.[5] have found, in 80 cases (mostly in adults) treated at St. Mary's Hospital, London, a strikingly high incidence of damage to the spinal cord. In 15 spinal block developed, and 10 had one or more attacks of transverse myelitis; two-thirds of all the patients with spinal block died. Careful pathological studies showed that unresolved exudate, with its associated vascular lesions, accounted for most of the damage. The St. Mary's workers find that improved chemotherapy has not affected the incidence of this severe complication, and they "emphatically support" the view of WINTER [6] that an effective agent for the dispersal of exudate is needed both for prophylaxis and for treatment. They do not mention tuberculin as a possible agent; but, as TAYLOR has pointed out, P.P.D. (purified protein derivative) tuberculin seems to have the necessary properties. Transverse myelitis does not seem to have been common in the Oxford series of adult patients, who received P.P.D.; and in view of the report from St. Mary's further detailed analysis of the effect of this substance on the incidence of lesions of the spinal cord would be valuable.

1. Lorber, J. *Lancet*, 1954, i, 1104.
2. Lorber, J. *Ibid*, p. 1149.
3. Taylor, K. B. *Tubercle*, 1954, 35, 126.
4. Ogilvie, H. *Lancet*, Aug. 28, 1954, p. 395.
5. Brooks, W. D. W., Fletcher, A. P., Wilson, R. R. *Quart. J. Med.* 1954, 23, 275.
6. Winter, W. J. *Amer. Rev. Tubere.* 1950, 61, 171.

The treatment of tuberculous meningitis is long and painful for the patient, and demands unremitting attention from doctor and nurse. Any ill-advised metabasis may result in death or idiocy. Attempts to eliminate intrathecal therapy [7] or to reduce the length of treatment are justified only if undertaken cautiously in specialised units. Doctors working outside the specialised centres have one crucial duty: to diagnose the disease in its earliest phase. Any insidious illness with headache and drowsiness or irritability may be due to early meningitis. When there is any suspicion of meningitis, lumbar puncture should be done without delay. Whenever possible cases should be admitted to a specialised unit.

Annotations

ROAD ACCIDENTS

IN Britain between 1940 and 1945 road accidents accounted for 42,137 deaths; air-raids over the same period were responsible in all for 58,881 deaths. Air-raid deaths declined over the period (apart from the flying-bomb peak in 1944) but road deaths maintained a steady level and are with us still, to the tune of some 4000 fatal accidents a year. The non-fatal injuries, of course, far outnumber these; and road casualties as a whole are estimated to cost us about £100 million a year. Mrs. Barbara Preston who quotes these figures in a new book [8] is out of sympathy with this death roll, and with the complacent way in which we suffer it to continue. She proposes some comparatively inexpensive remedies which—though they would inconvenience some—could be trusted, she believes, to reduce drastically the death and injury rates.

We do not all run the same risks on the road.

Far more pedestrians are killed than any other kind of road user: in 1950, 44% of all those killed were pedestrians. Males are killed more often than females: "the most vulnerable age and sex on the roads are men aged 15 to 30." Among children aged 5–10 road accidents are by far the commonest cause of death. Nearly a quarter of all those killed in 1950 were motor-cyclists, pillion riders, or passengers in sidecars; 16% were pedal-cyclists. Only 7%, 5%, and 2% were killed in motor-cars, goods-transport vehicles, and buses respectively.

Thus, those who ride inside vehicles are far safer than those who walk, bicycle, or travel by motor-cycles; which means, of course, that in common decency drivers of vehicles ought also to be specially careful. Goods-transport vehicles have the worst killing record, and are particularly deadly to children. In 1949, of 632 children under ten who were killed on the roads, 59% died from accidents in which goods-transport vehicles were concerned.

We have good legislation to deal with motoring offences, but Mrs. Preston holds that the fines commonly imposed by magistrates are too small to act as a deterrent. The average for all offences is only 35*s.*; and the average for using a vehicle with defective brakes, tyres, or lights (faults which the police held to have contributed to 4780 personal-injury accidents in 1951) is only 22*s.* She believes strongly in the value of propaganda, which should freely accompany any new legislation or road-safety plan. This has been the principle followed at Salford, where the annual road accidents were reduced from 730 in 1928 to 395 in 1935. The emphasis was on local events. School-children took home to their parents leaflets giving particulars of accidents to local children;

7. Douglass, B. E. *Proc. Mayo Clin.* 1953, 28, 171.
8. Forus on Road Accidents. London: Public Affairs News Service. 1954. Pp. 79. 7*s.* 6*d.*

and the cinemas showed the same particulars on their screens. They also included in their programmes films showing how local children behaved when crossing the street, and illustrating good and bad behaviour at crossings. Salford was the first town to set aside play streets for the use of children. Mrs. Preston emphasises the value of speed-limits—not only fixed limits for heavy vehicles, but limits for all traffic passing through towns.

The most striking example she cites comes from Providence, U.S.A., where a limit of 25 m.p.h. is rigidly enforced. It was given a trial period in which motorists offending against it were warned or prosecuted, or had their licences suspended for a time, according to their offences; and there were enough police to catch the offenders. In six months the road deaths had fallen to half the figure for the same period in the previous year, casualties were reduced by 60%, and Providence had become the safest city for road-users in the United States. The intention had been to try the limit for sixty days, but the police staged a small experiment: two cars crossed the city, one driver observing all the rules of good driving including the speed-limit, the other driver speeding, trying to "beat the lights" and using every trick for haste. The first driver took 17 min. 22 sec. to get through the city, the second 16 min. 8 sec. The citizens of Providence decided that the risk involved in saving 1 min. 14 sec. was too great, and that they would make the speed-limit permanent.

Mrs. Preston proposes that more—perhaps twice as much—should be spent on propaganda, that road research should be extended, that local authorities should have more to spend on local road-safety measures, that road-safety legislation should be far more vigorously enforced, that periodical inspection of vehicles for road-worthiness should be compulsory, that all vehicles should carry lights which would make it possible to detect when they were breaking the speed-limits, and that motor-cyclists should be compelled to take a training course. She would also like to see more effective ways of detecting the driver whose reactions have been slowed by alcohol, and believes that periodical medical fitness and driving tests might materially reduce accidents. There is probably a good case, she thinks, for setting up special traffic courts. Meanwhile more islands, guard-rails, traffic-wardens, and parking-places and better road layout may all save lives. Few of the measures she advocates are costly, and if all were applied they might cut down accidents by as much as half. Quite apart from the saving of life and health which this would mean, it would also greatly reduce the present high cost of accidents in hospital and medical care.

TINEA CAPITIS

SHOULD children with scalp ringworm be kept from school? Dermatologists are still exercised by this question. To send the children to special hospitals where they can be taught (as at L'école Lailler in Paris) is expensive; and the quickest mode of treatment—X-ray epilation—involves disproportionate risks. Attempts have therefore been made to assess the advisability of allowing children to attend school while undergoing simple local treatment.[1] Opposition to such a scheme has usually come from school and public-health authorities, who naturally wish to minimise the risk of infection; so it is heartening to read in the *Medical Officer*[2] that "exclusion from school should be carefully considered before it is enforced."

The feasibility of simple local treatment and uninterrupted school attendance depends somewhat on the organism. The common human species, *Microsporum audouini*, is the usual cause of epidemics; the animal species, *M. canis*, generally gives rise to small outbreaks, often limited to families. Case-to-case spread of *M. canis* undoubtedly occurs, but the organism rapidly loses virulence. Moreover, spontaneous cure is much commoner with *M. canis* than with *M. audouini*; which may account for the greater success of simple local therapy of infections with *M. canis*.

Everall[3] has reported 205 cases of tinea capitis treated at the Leeds General Infirmary between 1950 and 1952. Two-thirds were due to *M. canis*, and the majority of these responded to simple local treatment; only about 7% required X-ray epilation. Of the remaining third, the *M. audouini* group, more than half required radiotherapy, because of persistent infection. Everall recommends a trial of simple treatment for three months; if infection persists X-ray epilation should be carried out. Two-thirds of the *M. canis* group, and a quarter of the *M. audouini* series, were cured in under three months; this is no longer than the time required for X-ray treatment and pronouncement of cure.

Everall's study confirms the good prognosis in many cases of scalp ringworm, but it does not help in deciding whether infected children should be sent to school. Everall's cases and contacts were kept away from school until two negative examinations, separated by an interval of a month, had been recorded. This may be a sound preventive practice. But, as the *Medical Officer* says, is the risk at school, where children spend perhaps five hours of the twenty-four five days a week for only part of the year, greater than that outside?

INTERNATIONAL STANDARDS

IT is taken for granted nowadays that medicaments are of known and reproducible potency, so that the patient receives the prescribed dose. To achieve this state of affairs much work has been done by manufacturers and control authorities. Drugs of known chemical composition present no great problem. The real difficulties arise with biological products of which the potency is defined in terms of arbitrary units. In this country the Therapeutic Substances Act defines the units of many biological substances, and the label on an ampoule describes accurately the potency of the contents. Until recently, however, a unit of tetanus antitoxin on one side of the Atlantic Ocean had only half the value that it had on the other.

The health organisation of the League of Nations adopted an international unit, and offered a standard preparation, of diphtheria antitoxin over thirty years ago. This international coöperation has continued ever since, and the World Health Organisation now has 59 international standard reference preparations. For accurate measurement in terms of units, comparison with standard preparations is essential; and in this field the pioneer work of Sir Henry Dale and Sir Percival Hartley has been developed by their successors in the Department of Biological Standards of the Medical Research Council.

The latest issue of the *Bulletin of the World Health Organisation*[4] contains eleven articles on international standards. It is not easy to draw general conclusions from such diverse studies, but two trends are noteworthy. The first is the welcome extension of standardisation to diagnostic reagents. It may be just as important to the patient that his disease is accurately diagnosed as it is that the drugs he receives in treatment are accurately standardised. The second trend is towards the development of international standards for biological substances used primarily in the veterinary field. The eradication of brucellosis from dairy herds is obviously important for the public health, and this is aided by the use of an internationally standardised anti-*Brucella abortus* serum for the examination of agglutinating suspensions.

1. *Lancet*, 1953, ii, 716.
2. *Med. Offr*, 1954, **92**, 26.
3. Everall, J. D. *Ibid*, p. 29.
4. *Bull. World Hlth Org.* 1954, **10**, 867.

PAINLESS MYOCARDIAL INFARCTION

How commonly is myocardial infarction painless? Parkinson and Bedford[1] emphasised in 1928 that in established heart-failure dyspnœa might overshadow pain. Morton et al.[2] reported a series of 35 postoperative infarctions nearly two-thirds of which were painless, whereas Warner[3] found that pain was present in each of 200 cases of infarction. Roseman[4] points out that pain may be overshadowed by faintness, syncope, or acute dyspnœa (as noted by Papp[5]), and that the severity of the pain may vary considerably: it may be agonising, or no more than an ache or sensation of tightness in the chest. In Roseman's series of 220 cases 10 had apparently no pain or discomfort, but only 5 of these patients gave reliable histories.

The reason for the absence of pain is sometimes obscure. Pain may be masked by other symptoms or by impaired consciousness, or morphine may have clouded the memory; but these explanations do not always apply. Keefer and Resnik[6] thought that in patients with a slow infarction the pain impulses might not be sufficiently intense to reach the sensorium, while Herrick[7] suggested that anoxia of the myocardium, by destroying the sensory nerve-endings, blocked the pain response. In a small proportion of cases—no more than 1–2%—there are no symptoms at all. The diagnosis is then made only on routine cardiography or at necropsy if the patient dies from another cause. Myocardial infarction may manifest itself in several ways: by acute or progressive dyspnœa; by syncope[5]; by angina of effort[8]; by congestive cardiac failure; by hypotensive circulatory failure; or by arterial embolism.[9]

SELF-INDUCED EPILEPSY

Berger's early work on electro-encephalography (E.E.G.) included "driving" the rhythms he obtained from occipital electrodes by flashing into the patients' eyes a light of slightly different frequency to that of the spontaneous rhythm. This type of photic stimulation has been used experimentally, especially by Grey Walter and his colleagues,[10] and it has been found to cause changes in mental state and, occasionally, undoubted epileptic attacks. Recently the clinical implications of such stimulation have been recognised.

Cobb[11] in 1947 described three cases of visual-reflex epilepsy in which the effective stimulus was a naturally occurring interrupted source of light—in one case sunlight interrupted by trees as the patient drove along a road, in another the flickering of a street-light due to a faulty contact. Both Gastaut[12] and Bickford[13] have since recorded instances of children who purposely induced fits by submitting themselves to an intermittent light stimulus; and Graeme Robertson[14] has now recorded seven further cases of this self-induced epilepsy. In these seven cases the majority of attacks were of petit mal, though grand mal did occur; and the E.E.G. accompaniment was generally of the wave and spike type at 3 cycles per second. One point on which Robertson does not comment is the almost compulsive urge of these patients to induce attacks by passing the hand before the eyes in bright sunlight—even when the occurrence of an attack was a source of shame and disapproval. It seems almost as if this method of depressing cerebral function can become as habit-forming as that other group of cerebral depressants, the drugs of addiction.

1. Parkinson, J., Bedford, D. E. *Lancet*, 1928, i, 4.
2. Morton, A. M., Dack, S., Jaffe, H. L. *J. Amer. med. Ass.* 1938, **110**, 1415.
3. Warner, H. R. *Minn. Med.* 1951, **34**, 49.
4. Roseman, M. D. *Ann. intern. Med.* 1954, **41**, 1.
5. Papp, C. *Brit. Heart J.* 1952, **14**, 250.
6. Keefer, C. S., Resnik, W. H. *Arch. intern. Med.* 1928, **41**, 769.
7. Herrick, J. B. *Amer. Heart J.* 1931, **6**, 589.
8. Wade, E. G., Morgan Jones, A. *Brit. Heart J.* 1951, **13**, 319.
9. Lary, B. G., de Takats, G. *J. Amer. med. Ass.* 1954, **155**, 10.
10. Walter, W. G., Dovey, V. J., Shipton, H. *Nature, Lond.* 1946, **158**, 540.
11. Cobb, S. *Arch. Neurol. Psychiat.* 1947, **58**, 70.
12. Gastaut, H. *Rev. Praticien.* 1951, **1**, 105.
13. Bickford, R. G., Daly, D., Keith, H. M. *Amer. J. Dis. Child.* 1953, **86**, 170.
14. Robertson, E. G. *Brain*, 1954, **77**, 232.

IMMUNISATION

THE wide success of immunisation has certainly not made immunologists complacent; for healthy controversy still surrounds the differences in procedure between different countries. It is interesting to compare the methods recommended at a symposium on pædiatrics arranged by the American College of Physicians[1] with those discussed at a meeting of the Royal Society of Medicine[2] in London earlier this year and at a World Health Organisation conference[3] in Yugoslavia in 1952.

Top,[1] of Iowa, favours mixed prophylactics containing multiple antigens, and apparently does not consider dangerous the alum in prophylactics containing pertussis vaccine, which in this country is suspected of predisposing to paralysis in poliomyelitis. He suggests that single antigens should be used only in exceptional circumstances, since multiple antigens are apparently only slightly more liable to produce toxic side-reactions and the adjuvant effects increase antibody production. American pædiatricians strongly favour tetanus immunisation in infancy, with repeated booster doses of tetanus toxoid; injured children are given a booster dose of toxoid in addition to tetanus antitoxin. Since whooping-cough is so dangerous in early infancy pertussis immunisation by this American plan is begun at 4–6 weeks, and is followed by inoculation of a mixed pertussis-diphtheria-tetanus prophylactic four weeks later, and at 4 months, 5 months, 18 months, and 5 years. If a mother is Schick-negative diphtheria toxoid is not included in the prophylactic mixture until the infant has reached the age of 5 months. Smallpox vaccination is recommended between 6 months and 1 year of age.

Even with multiple prophylactics, the course of injections by this plan will make the first year of the infant's life a busy one, and close coöperation between parents, doctors, and medical administrators will be necessary if a worth-while proportion of the infant population is to be fully immunised against whooping-cough, diphtheria, tetanus, and smallpox. Immunisation against scarlet fever is now less often practised; but measles, mumps, influenza, and poliomyelitis vaccines may become widely used, and vaccination against yellow-fever, cholera, and typhoid is becoming commoner. The bottle of medicine, it seems, is gradually being supplanted by the ampoule and syringe.

AMYLOIDOSIS AND ENDOCRINES

THE experimental formation of amyloid by subcutaneous injections of sodium caseinate is apparently enhanced by maintaining the animals at an artificially high temperature. Perāsalo and Latvalahti,[4] who made this observation, found that the animals' adrenal glands, spleen, liver, and kidneys showed changes which, they thought, were due to the "adaptation syndrome"; so they investigated the influence of hormones on experimental amyloidosis. Corticotrophin increased the incidence and amount of amyloid in mice treated with sodium caseinate; cortisone and adrenocortical extract had a similar but less distinct effect; but deoxycortone had apparently no effect. Testosterone had no effect in intact

1. Top, F. H. *Arch. intern. Med.* 1954, **41**, 305.
2. See *Lancet*, 1954, i, 299.
3. *Ibid*, 1953, ii, 125.
4. Perāsalo, O., Latvalahti, J. *Acta path. microbiol. scand.* 1954, **34**, 208.

animals, but castration increased the incidence of amyloid. Thyroid-gland extract did not enhance amyloid formation. On the other hand amyloidosis developed in all thyroidectomised animals which had received sodium caseinate.

These results suggested that the pituitary-adrenal system had a pronounced influence on amyloid production. Perăsalo and Latvalahti deduced that the thyroid secretes a substance which inhibits the elaboration of amyloid. This, they thought, might be the end-result of stress causing adrenal hyperfunction with consequent atrophy of lymphoid tissue and hypertrophy of reticulo-endothelial structures. Hyperglobulinæmia develops, and as "resistance is simultaneously lowered, precipitation of amyloid" takes place, possibly because of exhaustion of antibody production and excess of antigens in the blood.

Any explanation of amyloid formation must take into account both the absence of amyloidosis in many chronic suppurating conditions and the occurrence of atypical amyloidosis unassociated with chronic inflammations. It will be interesting to see whether amyloid disease, at present rare, becomes more common with the increasing use of cortisone in chronic infections.

HEALTH IN EAST AFRICA

PERHAPS the greatest barrier to the development of Africa's natural resources is the prevalence of disease. The medical programmes of all African countries are restricted by the dearth both of skilled personnel and of money. It is therefore very important that existing resources for preventing disease should be applied where they will do most good. Commonly the African harbours several species of parasites, each of which may affect his health differently; and the predominant pathological parasites vary between one region and another. To study these problems the East African Medical Survey was set up, with headquarters at Mwanza in the Tanganyika Territory section of Lake Victoria.[1]

In the first of two papers by members of the staff, which was published a week or two ago, Dr. Trant[2] described the great variety of food taboos among Africans. A few of these taboos may have arisen from sensible and practical public-health ordinances; but the great majority are derived from irrational fears, and almost all prevent the best use of the limited food-supplies. During pregnancy and lactation a mother needs both more food and better food, and yet it is precisely at this time that taboos are most stringent. Clearly no programme for maternity and child-welfare services or for nutrition is likely to make much progress while the lives of so many women are dominated by such irrational practices. In East Africa a detailed study of food taboos and of means of ousting them should be in the forefront of the medical programme. Modern medicine can do little for a population whose lives are built on fear of unknown spirits and demons.

In the second paper, which appears on p. 801 of this issue, Colonel Laurie, director of the survey, considers the effects of intestinal parasites on health. He points out that infestation with various intestinal parasites does not necessarily interfere greatly with health: it is the intensity of the load that is important. Apparently in many parts of Africa patients are infested with intestinal parasites in abundant variety but in insufficient numbers to cause gross ill health.

The annual reports show that studies of the prevalence and intensity of filarial, malarial, venereal, and leprous infections are in progress. The latest report shows that there are five vacancies on the establishment of the East African Medical Survey. Any young doctor who is accepted for one of these posts will find plenty of fascinating and useful work.

1. Annual reports for 1952 and 1953 are obtainable from the Government Press, Nairobi.
2. Trant, H. *Lancet*, Oct. 2, 1954, p. 703.

MESTINON IN MYASTHENIA

NEOSTIGMINE, introduced by Mary Walker in 1935 for the treatment of myasthenia gravis, is one of forty-three analogues of physostigmine prepared by Aeschlimann and Reinert.[1] Only a few of these analogues were then available for clinical trial; and soon afterwards one of them, no. 36 of the series, was found by Laurent[2] to have useful antimyasthenic properties.

The two chief disadvantages of neostigmine are its undesirable side-effects, such as gastro-intestinal colic, and its relatively brief action. A new analogue has been introduced in America under the name of 'Mestinon.' This is the dimethylcarbamate of 3-hydroxy-1-methyl-pyridinium bromide. Some favourable clinical reports have appeared; and Osserman and Kaplan[3] have found that side-effects are fewer than with neostigmine, and that atropine is very rarely necessary to check colic. Mestinon has proved the more effective antimyasthenic agent in 12 of their 20 patients. This drug strengthens the small muscles of the eye and of deglutition better than the larger skeletal muscles; whereas the reverse is true of neostigmine. This may influence the choice of drug in a given case. The two drugs act for about the same time; but some patients claim that mestinon acts longer, since many hours after the last dose they wake up stronger than usual.

Blaschko et al.[4] have found that mestinon has only an eighth the anti-curare and a tenth the anti-cholinesterase activity of neostigmine. Clinical experience shows that the antimyasthenic action of neostigmine is about four times that of mestinon, and tablets containing 60 mg. of the new drug correspond to the usual neostigmine tablet of 15 mg. The results of limited trials in this country agree generally with those of Osserman and Kaplan, but patients here usually say that the 60-mg. tablet of mestinon is weaker than the 15 mg. of neostigmine: it causes less toxicity but it also relieves myasthenia somewhat less strongly.

The new drug should be tried by any patient who is not doing well with neostigmine, but its advantages are not so clear that it should be given to patients well controlled by the older drug.

BIO-ASSAY OF STEROIDS

MUCH is known of the relation of steroids to the gonads, but so far little attention has been paid to the effect of different steroids on the growth of the uterine and vaginal membranes. Huggins et al.[5,6] have found in hypophysectomised rats that the mucous membrane of the vagina and uterus, which is normally sensitive to œstrogenic and progestational hormones, also responds to many compounds closely related to the androgens. Some of these compounds affect both the rate of growth and the type of growth; some steroids promote growth of the superficial cells of the vaginal epithelium and stimulate secretion of mucoprotein, whereas others affect deeper cell-layers and cause keratinisation.

This method promises to yield information unobtainable by standard methods of bio-assay. Further such studies may provide a more rational approach to the treatment of endocrine disorders, and remove some of the uncertainties of hormone therapy.

1. Aeschlimann, J. A., Reinert, M. *J. Pharmacol.* 1931, **43**, 413.
2. Laurent, L. P. E. *Brit. med. J.* 1935, i, 463.
3. Osserman, K. E., Kaplan, L. T. *J. Amer. med. Ass.* 1954, **155**, 961.
4. Blaschko, H., Bülbring, E., Chou, T. C. *Brit. J. Pharmacol.* 1949, **4**, 29.
5. Huggins, C., Jensen, E. V., Cleveland, A. S. *J. exp. Med* 1954, **100**, 225.
6. Huggins, C., Jensen, E. V. *Ibid*, p. 241.

Special Articles

SURVEY BEFORE SERVICE
OBSERVATIONS ON RELATION BETWEEN AGRICULTURE, PARASITE LOAD, AND NUTRITION ON A TROPICAL AFRICAN ISLAND

WILLIAM LAURIE
D.S.O., M.D. Glasg., T.D.D., Lieut.-colonel I.M.S. retd
DIRECTOR, EAST AFRICAN MEDICAL SURVEY

MEDICAL surveys, properly conducted, are expensive; *but their expense may be fully justified when the* information they provide shows how to make the best use of the small amount of money available for the control of disease, and when it prevents much of this money from being spent on the control of conditions which may in fact be relatively unimportant to health. Without exact local information the emphasis of our *efforts may be wrongly placed. For example, Trant's* inquiries[1] have shown that, if we are to improve the nutrition of African women we must pay attention not only to food-supplies but also to food taboos. Similarly the facts obtained in a recent investigation in Ukara, which forms part of the work of the East African Medical Survey, suggest that if agriculture is good, nutrition can *be good even when the parasite load of the population* is heavy.

The Ukara Survey

Ukara Island lies in the Tanganyika section of Lake Victoria. Much of its scenery is dour and forbidding, consisting of rocky hills with little vegetative growth, and only 13½ of its 30 sq. miles is fit for cultivation. But despite its poverty and small size it supports a population of almost 17,000—an average of 600 souls to *the square mile.*

In early 1950, when our investigation began, Ukara was almost completely cut off from the mainland. The nearest medical and administrative centre was two days' (very risky) sail across the Lake. For years the people had been left to their own devices except for occasional brief visits from European officials. Latterly these had brought back alarming reports about the state of the health of the Wakara. The people were said to be hungry —a reasonable assumption in view of the population pressure and the poor soil; they were thought to be suffering severely from the effects of intestinal para*sitism; hydrocele and elephantiasis were described as* extremely common; and Dr. Ross Innes, the inter-territorial leprologist, had found leprosy in 256 persons, or 1·5% of the population. There was good reason to believe, therefore, that the people were ill and in urgent *need of much medical help.*

METHODS

We examined 3677 people (20% of the population) drawn at random from both sexes and of all age-groups. Besides a physical examination we made a pathological examination of each person, including examination of *blood-films, hæmoglobin levels (grey-wedge, checked by* Sahli), stool examination, urine examination, and Kahn *reactions of the serum. We also took the obstetrical* histories of all the women over fifteen years of age and we kept birth and death registers. Supporting investigations included a veterinary survey and tuberculin surveys, and we also set up dispensaries.

PHYSICAL FINDINGS

Hair

Hypochromotrichia was found in 209 (11·2%) males and 66 (3·6%) females, but only at ages below twenty. This finding should be regarded with caution, for Usborne[2] has reported hypochromotrichia in young healthy males showing no stigma whatever of malnutrition.

Eyes

About 1 person in every 30 was blind in one eye, usually as a result of measles or smallpox. During a measles epidemic on the island the physician saw many cases of advanced purulent conjunctivitis and neglected corneal ulceration. Eye conditions are badly treated at dispensaries and by the witch-doctors, and one of our medical staff suggested that witch-doctors should be taught the proper handling of eye lesions. This suggestion is not so wild as it seems, for the witch-doctor has a much larger clientele and a much higher social standing than government dispensers.

Lips

Cheilosis was found in 357 (19·2%) males and 174 (9·6%) females. It is commonest in the early teens.

Abdomen

Spleen enlargement was present in 36% of the people examined. Those with enlarged spleens were on the average 4 lb. lighter in weight than those without. Liver enlargement was found in 3% of the population. Abdominal hernia was common.

Hydrocele

The over-all incidence of hydrocele among males is 8%, its incidence rises with age to as much as 24% of the total male population over sixty. In our opinion the importance of hydrocele as a complication of bancroftian filariasis has been underestimated.

Elephantiasis

The high prevalence of elephantiasis of the lower limbs—50 (2·7%) of the men and 72 (4%) of the women—is in keeping with the high incidence of hydrocele and is a measure of the *intensity of bancroftian infection on the island. In men with* hydrocele or elephantiasis, the blood-pressure was commonly higher.

LABORATORY FINDINGS

The analysis of the laboratory findings is limited to a random smaller group inside the whole sample of 3600 people.

Intestinal Parasites

Of the 790 records so far analysed only 5 (0·6%) people *were free of infection. Multiple infections were frequent.* The commoner parasites were hookworms (38% incidence), ascaris (36%), *Entamœba coli* (60%), *I. butschlii* (45%), *Schistosoma mansoni* (36%), *Strongyloides stercoralis* (15%), tapeworm (4%), *Trichuris trichuris* (52%). Other parasites found were *Ent. histolytica* (5), *Ent. histolytica* cysts (1), and *Giardia lamblia* (21). Probably all these figures are lower than they should be, for they are based on examination only of a single twenty-four-hour specimen of stool.

Urinary Schistosomiosis

The incidence of these parasites was found to be only 2%.

Blood-borne Parasites

Relapsing Fever.—In all 8000 blood-films were examined, 1 blood-film for almost every second person on the island. Only in 18 patients was relapsing fever found, and each was a dispensary patient.

Filariasis.—The only filarial infection found was bancroftiasis, which was extremely common. The incidence of *microfilaræmia was:*

Age-group	*Patients*	*Incidence*	*Age-group*	*Patients*	*Incidence*
5–10	568	6%	21–40	2018	35·2%
11–15	1046	7%	*Over 40*	*806*	*36·8%*
16–20	1463	8·4%			

The night blood-films were taken at 10 P.M., and the true incidence of microfilaræmia is almost certainly much higher than the figures given.

Malaria.—An examination of thick and thin films from seemingly healthy Wakara showed that in the younger age-groups half the films contained scanty malaria parasites. The incidence of positive films fell as age increased.

Hæmoglobin Levels

The mean hæmoglobin content in the various age-groups ranged from 70·7 to 87·8%. The levels are below standards

1. Trant, H. *Lancet*, Oct. 2, 1954, p. 703.

2. Usborne, V. M. *E. Afr. med. J.* 1954, 31, 55.

accepted as normal for healthy Europeans; this is especially true when it is remembered that Ukara Island lies at a height of 3700 feet, and that correction must therefore be made for height.

Serological Reactions

The results of over 1000 Kahn reactions are available so far. Even when single-plus reactions and all cases of leprosy, malaria, and other complicating conditions are excluded, the findings are high:

—	No. examined	Reaction ++	Reaction +++
Men	487	11·5%	4·31%
Women	492	9·76%	4·88%
Children	46	13%*	..

* 1 malaria.

VITAL STATISTICS

Information was obtained by questioning 2579 women, almost two-thirds of all the women on the island. A cross-check on the figures was obtained by keeping birth and death records.

The current total fertility-rate was estimated at about 4·1 to 4·4. Of the children, 25% died before the age of five, and 30% died before the age of twenty-two. The net reproduction-rate was 1·4—i.e., a fairly fast increase of about 1·2% per year. At this rate the population would double itself in about sixty years.

MORBIDITY

Among 1216 consecutive patients attending one of our dispensaries almost 70% of the attendances fell into the following four groups:

"Abdominal pain" (102 patients), diarrhœa (44), ascaris (64), and hookworm (26) accounted for almost 20% of attendances.

Another large group of 15% was probably due to the effects of the cold wet rainy season on the ill-clad islanders—i.e., pneumonia (12), cough (99), bronchitis (26), and pain in the chest (40).

A third group, also 15%, was malaria (47) and "fever" (132), and, as was to be expected, almost 80% of these patients fell into the under-five age-group.

A fourth large group, which might well have been included with the malaria-plus-fevers, was that of enlarged spleen (110). Here again 60% of the patients were under-fives.

Scabies and tropical ulcer were uncommon and fewer septic skin conditions were found than is usual in dispensary work, probably because the islanders have unlimited supplies of fresh water and bathe often.

It must be remembered that dispensary attendances alone do not give a true picture of the diseases of the people. For example, among the 1216 consecutive patients less than 2% were suffering from venereal diseases compared with a likely total of about 15%: filariasis patients were few indeed, although at least 30% of the population are affected; and only 5 lepers were seen although there were known to be 256 on the island.

Discussion

These findings show that the Wakara have their full share of troubles. The island is much overpopulated: the tropical infections are extremely common; and the people are poor. Yet the Wakara height/weight ratio for males is 1·95, which is the third highest among the fit males of the 31 tribes, whose heights and weights have been recorded by the East African Statistical Department. In other words despite minor signs of vitamin deficiency, and somewhat unsatisfactory hæmoglobin levels, the Wakara cannot be regarded as a people suffering to any significant degree from undernutrition either direct or due to disease. In the words of one medical survey officer, "the Wakara lead satisfying, hard-working lives of great happiness." This finding is in striking contrast to what was expected, so much so as to justify full consideration of the reasons for the happy state of affairs.

Briefly the answer lies in the fact that under the spur of that most potent of all stimuli—famine—the Wakara have evolved a system of agriculture unique for Africa. According to Rounce and Thornton,[3] the basic reason for their success is the fact that, unlike other African stockholders, they tend their cattle as an essential part of their system of farming and not as a means of storing wealth. There are 9892 cattle and 4833 sheep or goats on the island—i.e., 11,000 stock units for 3680 homesteads, an average of 3 stock-units per homestead. Natural grazing is poor and the cattle are bedded down and hand-fed inside the owner's hut: to prevent their eating crops en route the cattle are muzzled when taken to water. From time to time the semi-decomposed bedding is taken from the huts and heaped outside to undergo desiccation: it is later applied to the land. Also the islanders grow and dig in a green-manure crop: they practise rotation of the crops and the growing of forage crops. Great care is taken to prevent soil erosion. These practices, very advanced for Africa, have enabled the Wakara to maintain a population greatly in excess of those in much more fertile areas. The island is three times as densely populated as the most crowded part of the neighbouring mainland.

Conclusions

The first lesson learnt from the Ukara survey is the importance of carrying out a detailed, properly planned survey before undertaking any large schemes to control disease. Such a survey may show that the people will gain far more from resettlement or agricultural development than from new hospitals and schemes for eradicating diseases.

Secondly, this survey showed once more the futility of using the results of parasite surveys as a measure of estimating the state of health of a population. It is not unusual to find a seemingly healthy African harbouring so many parasites as to be almost a museum in himself. The important problem is not whether or not infection is present, but to what degree it is present. Until the pathologist evolves methods of measuring the intensity of infections the results of parasite surveys will give no indication of the harm, if any, such infections are causing. Thus, in our 1951 annual report [4] we showed that there is no relation between hookworm infections and anæmia, except when the hookworm-load is very high.

Lastly, the Wakara have shown that, even where the soil is poor, the answer to food shortage may often be found in a satisfactory system of mixed farming. In spite of some opinions to the contrary, the informed view still is: "cattle wrongly used are the bane of agriculture: rightly used they are its blessing."

3. Rounce, N. V., Thornton, D. Tanganyika Notes and Records. Dares Salaam, 1936.
4. East African Medical Survey Annual report, 1951.

"... We are again haunted by the ghost of Malthus; no one is quite sure how large a part heredity plays; whether improvements in human behaviour through environmental change are more than temporary; how far human happiness can be permanently increased by improvements in social welfare. Most important of all, we can no longer put so much trust as our eighteenth-century forebears did in Reason. We have learnt to see ... that human history is not a steady evolution guided by ideas, but rather a struggle of social groups in which ideas have been selected by irrational desires, themselves the product of material forces. Worst of all, we have learnt how, in days of centralized power, the control of the radio and other means of 'mass communication' may enable our dictators to produce a degree of mental conformity of which mankind had never dreamt before and to which 'education' is not, in itself, an answer."—*Times Literary Supplement*, Sept. 10, 1954, p. 566.

The Wider World

RUSSIA REVISITED

Impressions of Soviet Medicine

T. F. Fox

M.A., M.D. Camb., F.R.C.P.

(*concluded from p. 753*)

III. THE STUDENT

In Tsarist Russia there were thirteen university faculties of medicine, and five medical schools for women; and about 1500 doctors qualified annually after five years' training. In 1930 the medical schools were dissociated from the universities and reorganised as part of the State medical service, becoming institutes under the ministry of health.[16] The U.S.S.R. now has sixty-three such institutes for medical students, with an output of 20,000–25,000 doctors each year.

They differ widely in both size and scope.

The 1st Moscow Medical Institute trains only two kinds of doctors—therapeutists and sanitarians—but it has 3700 students (of whom 600–700 qualify every year) and some 400 "aspirants" working for higher degrees. These Moscow students include many from distant places, such as Hungary, Czechoslovakia, Poland, China, and Viet-nam. The school has 1760 hospital beds of its own, and also sends its students elsewhere. It has fifty professorial chairs, and this year its staff have produced about 600 books and scientific papers.

The medical school at Tbilisi, the capital of Georgia, is relatively small but is more comprehensive in that it trains pædiatricians as well as therapeutists and sanitarians; and it also trains dentists and pharmacists. About 100 medical students enter each year, and some of their instruction is in Georgian.

Because many of the republics constituting the U.S.S.R. have their own languages and all have their own customs, the aim has been to distribute medical schools very widely, so that local people shall be trained for local work. But it has not always been possible to provide these schools with their proper quota of teachers and investigators, since many of the most competent men and women prefer to stay in the great cities of Western Russia; and there is evidence that some of the peripheral schools are quite inadequately staffed, besides having insufficient facilities for teaching. What is needed (one authority has pointed out) is not so much the creation of new schools as the strengthening and redistribution of those that already exist.

SELECTION

Some say that doctors are much respected in Russia; others talk of low remuneration and a general decline of status. Wherever the truth may lie, there seems to be no lack of candidates for training at the Moscow school we visited, where the acceptance-rate for applicants was this year only 1 in 9.

As the number accepted by this school is about 700, we must conclude that the claims of more than 6000 applicants are considered each year—a formidable task. Selection is partly intellectual, in that (unless they have won a gold or silver medal at school) all candidates must take a competitive examination (oral) in physics, chemistry, Russian language and literature, and "the elements of philosophy."[16] It is partly physical, in that they must be passed by a medical board, and there is a list of diseases that disqualify possible entrants to medicine. But the final decision must, I feel sure, take account also of the candidate's character, general abilities, personality, reputation, and opinions; and I did not myself understand how this final decision is made. No doubt the selectors in a Russian as in a British school are anxious to find the boys and girls most likely to make good doctors: but in a country where so much emphasis is on sociopolitical activity their conception of a good doctor may be rather different from ours. Some of them may share the view expressed by an official medical journal three years ago that "one of the most important duties of the faculties and schools of medicine is to build up cadres of Soviet intelligentsia in the spirit of Marxism-Leninism."[17]

Whatever the exact method of selection may be, it seems to satisfy the selectors; for we were told in Moscow that the services of a psychiatrist are seldom required for students and that of 700 starters the number failing to stay the course is likely to be no more than 50–60. At Tbilisi the total wastage was estimated at 5–6%.

STUDENT LIFE

Though the Moscow school will take students as old as 35, the vast majority enter at 17 on leaving school.[18] They mostly get a State stipend, ranging from 220 roubles a month in the first year to 290 in the fifth. For those who study well in all subjects the stipend is raised by 25%, and there are also additional grants and prizes, and funds for those in difficulties. In Moscow the students usually live in hostels, where the charge for lodging and laundry is only 16 roubles a month. Those who get married have separate quarters, but about 90% do not marry before they qualify. At Tbilisi first-year students sleep in smallish dormitories with half a dozen beds, while their seniors share austere little rooms for two. Food in the canteens is cheap, and the student borrows books from the library instead of buying them. In Moscow student scientific societies flourish: they teach (we were told) the principles and methods of scientific investigation, and the best papers by students are published by the school or even read at meetings in the city and published in the ordinary medical journals.[19]

The students are keen on sport, competing both at home and abroad, and many cultivate the arts. At Tbilisi they get two weeks' holiday in the winter and two months' in the summer. Students (I deduced) seldom if ever have to find money for their holiday expeditions or their sojourns in rest-houses or sanatoria.

THE CURRICULUM

Sigerist[20] described an experimental phase in Soviet medical education:

In the early 30s "methods of teaching were changed radically; most lectures were abandoned and were replaced by seminary and laboratory discussions. All teaching was what was called complex teaching. The barrier between anatomy and physiology, for example, was dropped and both subjects were discussed together. A case of illness was discussed not only from the clinical or pathological point of view but in all its complexity, including the social and economic factors involved. Students worked in groups, in teams. Upon entering medical school, four or five students joined to form such a team to work together throughout the course. It was believed that if one student was lazy, the others would make him work lest the group be weakened . . . At the end

16. Kurashov, S. V. *Brit. med. J.* Aug. 28, 1954, p. 510.

17. *Meditsinski Rabotnik*, Sept. 2, 1951. Translated from the French translation by Lazarévitch (*op. cit.* (ref. 3); p. 70).

18. In the cities, children go to school for ten years from 7 to 17. Under the present Five-Years Plan the school-leaving age for country children is to be raised to 17, but at present it is 14.

19. This sounds splendid. But Lazarévitch, alas, has again an apposite quotation (which I retranslate) from *Meditsinski Rabotnik* (Feb. 21, 1952) on the work of these societies. "Being a free organisation of students, which embodies the lively and gifted element of the youth of our great schools, the society takes its share in educating the students in the spirit of Soviet patriotism, in immutable loyalty to the homeland of Socialism, and in the relentless struggle against servile admiration of bourgeois science and culture." (*Op. cit.* (ref. 3); p. 73.)

20. Sigerist, H. E. *Op. cit.* (ref. 2); p. 56.

of the assignment, the group would present a joint report. Since Soviet medicine is group medicine, it was thought that the students should be trained early in this coöperative spirit.

"Final examinations were abolished again. The professors were required to judge whether the qualifications of a group were sufficient to allow its members to enter the medical service of the state."

But the medical curriculum, like so many other things in Russia, has since resumed a more conventional pattern.

In the first year the scientific subjects are chemistry, physics, biology, and anatomy: the student continues his study of the foreign language he learned at school (English, German, or French); in Moscow he learns a little Latin; and he is instructed in the principles of Marxism and Leninism. Political instruction continues into the second year, in which his scientific subjects are anatomy, histology, physiology, and biochemistry. In the third year he turns to pharmacology, microbiology, pathological physiology, morbid anatomy, and topographical anatomy. The ratio of practical work to lectures is about 2 to 1.

Entering the hospitals in their fourth year, the students form into groups of 10, and, as in Britain, are given their own cases in the wards. The Moscow school has adopted (so to speak) a region some 200 miles away, where its students, from the fourth year, work in district or village hospitals. The Moscow professors visit the region, and hold conferences there; the regional doctors work reciprocally in the Moscow school; and the arrangement is considered a very happy one. Remembering that "prevention is the red thread that runs through Soviet medicine," the students try their hand at lecturing on public health to the people of the region.

From his days in the physiology laboratory, the enterprising student may have taken part in some research project. In his sixth and final year before qualification he begins to follow his own bent in that he devotes his time chiefly to one particular branch of medicine—perhaps surgery, internal medicine, radiology, or gynæcology and obstetrics. This is termed "primary specialisation."

EXAMINATIONS

The Russian medical student must pass examinations every year in the subjects he has been studying; but all of them—even the final—are oral. ("I can't visualise a written examination," said one of the professors with whom we talked.) The "ordinary" examinations are conducted solely by the student's own teachers, but he also has to pass two "commission" examinations, in which he must satisfy a small examining board. The first of these is at the end of his second year, when the subjects are chemistry, biochemistry, anatomy, and physiology: Kurashov[16] describes this as a "semi-State examination" to determine the student's suitability for further study.[21] The second commission examination is the final State examination, at the end of the sixth year, and (at any rate at Tbilisi) the chairman of the examining board is someone from a distant medical institute. At each of the commission examinations the candidate must pass in four subjects; and, though he must satisfy the board as a whole, the questions will mostly be asked by a specialist in the given subject. At Tbilisi half an hour is allowed each student for each subject, but ten minutes commonly suffices. Full marks in each subject are 5 out of 5.

Students successful in the final are awarded either an ordinary diploma or else an honours diploma which entitles them, if they wish, to start at once on a three-year course of training as a specialist. But what happens (we asked) to students who fail their examinations?

Moscow.—The student who fails once has an opportunity to prepare a second time. (The reason for his failure was probably that he was ill.) If he systematically fails he is evidently unsuitable. But this is most exceptional: students are very strictly selected and as a general rule can cope with their work.

Tbilisi.—If he fails at the end of the first year he may take the subject again in the autumn; but if he fails this second time he must leave the school. In subsequent years, if he fails at the second attempt in the autumn, he must take the whole year's course again, omitting only any subject in which he got full marks (5). But very few are turned down: "our students are well disciplined and work well."

TEACHERS

The training of specialists and teachers has been outlined by Kurashov,[16] and here I need merely mention the rungs of the academic ladder.

By passing an open examination, the young doctor or more mature specialist may enter a special postgraduate institute, where his three years' study must include some research and where he prepares a thesis (which has to be publicly defended) for the degree of candidate of medical science. After two or three more years the candidate of medical science may present a thesis for his doctorate.

The titles of reader (dotsent) and professor are conferred or confirmed by a commission of the ministry of health and are retained for life; but the chairs that the professors occupy, or the posts that they hold at a research institute, fall vacant every five years and are then readvertised. The holder may be reappointed—or he may go home to live on his pension, "which is very high." In the Moscow school, all teachers must do some research.

I did not myself note any special developments in the technique of teaching. We were shown an excellent film on blood-transfusion for senior students and doctors; the Institute of Bone and Joint Tuberculosis near Leningrad was making a great variety of excellent wax models for distribution to medical schools; and there were museums of the familiar kind. But lectures seemed as prominent as ever, and at Tbilisi we were distressed to learn that a lecture consists of two periods, each of three-quarters of an hour, separated by only a few minutes' break. Though the students seemed cheerful, there was perhaps less obvious gaiety among the lecturers.

IV. THE INVESTIGATOR

The revolutionary rulers of Russia have been great believers in scientific progress, and the Soviet Union now has no fewer than 279 institutes for medical research. Some of these are large, and the range of their inquiries naturally defies summary. By way of sample, however, I shall say something about some of the work I heard about and saw.

WORK IN PROGRESS

Internal Medicine

Much attention is being paid to hypertension, and especially to the part played by the nervous system in its pathogenesis.

21. Up to this point the training of all medical students is the same; but from now onwards the curricula for therapeutist, pædiatrician, and sanitarian diverge. (Formerly the proportions in these groups were: therapeutists 75%, pædiatricians 15%, sanitarians 10%; but I omitted to ask what they are today). To amplify Kurashov's phrase "suitability for further study," I should perhaps quote the following account of an examination in anatomy:

"Most of the candidates showed much knowledge, and a remarkable capacity to make quick and judicious replies, to make clear the pre-eminence of Russian anatomists, to emphasise the priority of the national scientists, and to detect the errors and distortions of scientists in the reactionary camp." *Meditsinski Rabotnik*, Jan. 21, 1952; retranslated from Lazarévitch (*op. cit.* (ref. 3); p. 73).

In many if not all schools anatomy may now be taught in a purer form than this quotation suggests. But in studying Soviet medicine it would be unwise to ignore that portentous addition to medical school staffs—the professor of Marxism-Leninism.

As a form of preventive treatment, hypertensive workers may be offered places in night sanatoria where they can get peace and suitable food. Some members of our party were told that the atherosclerosis produced in rabbits by a high-cholesterol diet can be prevented by giving them ascorbic acid at the same time.

Surgery

Research continues on local anæsthesia for thoracic surgery. Experimental transplantation of organs is increasingly ambitious: whole extremities have been permanently grafted in dogs, and apparently a dog may survive as long as six days after having another dog's heart and lungs substituted for its own. The work of the late Professor Yudin on the artificial œsophagus (he performed 700 such operations) is being brilliantly continued at the Sklifassovski Hospital in Moscow. There, too, we saw an ingenious instrument for joining severed blood-vessels with tantalum wire clips. This can be applied to vessels of any diameter from 1·3 mm. to 15 mm., and with its aid more than 500 vascular anastomoses have been performed, we understood, without complication. Another instrument which inserts tantalum clips is used in pneumonectomy, for suture of the bronchial stump.

Neurology

One institute is particularly interested in the restoration of function after cerebral disturbance (e.g., hypertensive incidents). Sleep therapy is much studied now and widely used, though perhaps less widely than it was.

Poliomyelitis is "very rare" in the U.S.S.R., being least uncommon in the Baltic republics, Moldavia, and the Kazakh republic. Both gamma-globulin and adult serum are used in treating the acute stage.

Tuberculosis

The rôle of the nervous system in tuberculosis heads the list of subjects for investigation; but more immediately interesting is some work on primary infection, which has led to the conclusion that tuberculosis is a general infection from the beginning.

Though aware of "a certain scepticism" about B.C.G., the Russians use this vaccine on a large scale; and, as already stated, they go in for mass inspections for tuberculosis. Whether because of these measures or not, notifications have fallen by 20% "in the last few years," and mortality by 50%.

Cancer

At the Institute of Oncology in Moscow we were told that the commonest site of cancer is still the stomach (30%), followed by the uterus and the breast. Lung cancers are estimated at 6% or 7%, and no carcinogen has been detected in the Georgian tobacco generally used in Russia.

The work of the institute includes elaborate metabolic studies and chemotherapeutic experiments notably with an aliphatic derivative of nitrogen mustard and analogues of pyrimidines and purines. In the wards, analogues of nitrogen mustard (embikhin and novembikhin) are used for leukæmias, and five-year cures have been obtained with them in Hodgkin's disease.

Elsewhere we were given figures for five-year cures of cancer treated by combined methods: breast, 46% of 340 patients; uterus, 75% of 90 cases.

Industrial Hygiene

Silicosis remains a serious problem, but thanks to wet drilling and other measures new cases are now met with "very infrequently."

The Institute of Industrial Hygiene in Leningrad is doing impressive work especially on industrial ventilation, lighting, the effects of electrical fields, and noise. The investigations on noise cover the harm done by particular kinds of noise (e.g., in raising blood-pressure or lowering productivity), the means of preventing such harm, and the design of apparatus for measuring noise. For the use of factory inspectors a portable noise-meter has been designed, weighing 3 kg. and with a range of 55–140 decibels. Alternatively a tape recording of noise may be made at the factory and analysed in the laboratory. "Noise," said our informant, "is at present the only industrial hazard for which there is no prescribed limit." A national standard is now being laid down for lighting of factories, and special rules for special branches of industries; and a portable photometer can be taken to the scene of action. In another department apparatus is being made for the convenient estimation of noxious gases in industrial atmospheres.

Blood-transfusion

At the Sklifassovski Hospital, where Yudin collected cadaver blood for transfusion, this method is still employed: up to 1·5 litres can be taken from a body, and in twenty-five years 25 tons have been used—without complications or mortality. The Sklifassovski, however, is an emergency hospital with unusual sources of supply, and elsewhere it is customary to rely on donors who can still manage a cup of tea.

At the Blood-transfusion Institute in Leningrad a promising development is the use of freeze-dried conservants which make it possible to store blood at minus temperatures in the liquid state.[22] The advantages claimed are that the blood keeps longer, retains more gamma-globulin and other normal constituents, and is less likely to cause reactions. Much work is also being done on the biochemistry and metabolism of cells in stored blood. This includes the use of tagged atoms.

The blood substitutes prepared or studied at the institute include: a bovine plasma which is despeciated by heat and by biochemical methods and is said to be very widely infused with good results; dextran; polyvinyl pyrrollidone; an anti-shock solution; and a solution made from leguminous plants. Among the blood derivatives prepared are fibrin foams and films, and hard sticks of dried plasma which are on clinical trial as intramedullary pegs for joining fragments of a fractured bone.

In Leningrad, with a population of perhaps 3½ million, about 100,000 transfusions (normally of 250 ml.) are given annually. Mention was made of 70 icteric babies saved within two years by exchange transfusion. I have referred already to the elaborate but generous treatment of donors,[9] but I may add here that every donor has his photograph on his medical notes. A physician of our party wished that this were done for every patient everywhere.

Physiology

Though many branches of medical research have been affected profoundly by the emphasis latterly laid on the work of Pavlov, this is of course especially evident in the physiological laboratories, where Pavlov's methods are being developed most directly, according to plan. No laboratory was without its dogs.

PLANNING OF RESEARCH

Scientific research may be planned at any level, and there have been two occasions in the recent history of the Soviet Union when it was planned at a very high level indeed.

A compelling directive was given to Soviet biologists and agriculturists when in 1948 they were told to accept, as basis of their work, Michurin's view that the inheritance of acquired characteristics is "possible and necessary." Scientists in other parts of the world—though some of them agree with Michurin—were generally appalled to hear that because one biologist, Lysenko, had gained the ear of the authorities, and was preaching a convenient doctrine, other biologists who disagreed with him or remained unconvinced were being forced to conform or recant or disclaim what they really believed.

The second directive, by which the concepts of Pavlov were to be regarded as the theoretical basis of Soviet medicine, was perhaps even more political in origin. One need not look far to see that the explanation of human behaviour in terms of conditioned reflexes provides a scientific sanction for political indoctrination and for a materialist philosophy, while the dominance of the brain over every bodily activity may be regarded as a happy physiological parallel to the dominance of a central dictatorship.[23] This, however, is but speculation. What is unquestionable is that, after a joint conference of the Academy of Science and the Academy of Medical

22. This work was reported to the International Congress of Blood Transfusion held in Paris last month.
23. Lazarévitch, I. *Op. cit.* (ref. 3); pp. 19–40.

Sciences, held in the spring of 1950, a fresh course was set for medical investigation, using Pavlov as the guiding star. Not only were the schools of physiology and psychiatry instructed to reorientate their research and teaching on Pavlovian principles, but all possible opportunity was to be taken throughout medicine to study the rôle of the central nervous system in disease. Some of the results have been very interesting[24]; and nobody who knows anything about Pavlov's work would question the need to continue it and expand it. But, as in the Lysenko affair, the outside observer could do nothing but deplore the academic purge required for this reorientation of research—a purge involving several of Pavlov's old pupils who did not think that the master would have approved what was being done in his name.

Beyond the personal indignities and tragedies, we have to recognise the harm done to science whenever a scientific thinker is made to toe the line, and wherever merit is acquired by acquiescence rather than originality. In parting at last from Lazarévitch, whom I have employed so freely as *advocata diaboli*, I shall allow her one final comment—*this time in her own language*:

"... Faut-il rappeler aux héritiers frais émoulus de Pavlov la règle fondamentale de sa doctrine, à savoir que 'toute cellule placée sous l'effet d'excitations uniformes et constantes passe immanquablement à l'état d'inhibition ou entre en sommeil.' Cela peut aussi s'appliquer à l'organisme. En l'occurrence, il s'agit de la léthargie dans laquelle doit entrer nécessairement la physiologie russe soumise aux excitations uniformes et constantes du Kremlin." [25]

But the last word has not of course been said, in Russia or anywhere else. One of the characteristics—the terrifying characteristics—of an authoritarian State is that opinions and practice can be radically changed within a short time by a change of policy at the top: and there are signs that the group now leading the Soviet Union understand that, however much money is spent on science, it will never really flourish except in a scientific atmosphere—an atmosphere in which scientists are able to think and speak for themselves, initiate and plan for themselves, and criticise and be criticised without losing their jobs.[25]

In describing the current organisation of research our hosts showed themselves aware that organisation can be "just depressive," and they were at pains to explain that, despite planning, the medical investigator can follow whatever line he finds promising. The task of forming a general plan is entrusted to the Academy of Medical Sciences,[26] working in conjunction with the scientific council of the ministry of health, which controls all research institutes. Together they consider what are the problems most needing attention, and refer these to "problematic councils" which study what has already been done at home and abroad and construct a rational programme. Some 400 scientists take part in this planning, and the aim is to propose to each institute those investigations that are in line with its traditions and special capacities, and fit in with the particular interests of this or that investigator. A number of institutes will be asked, for example, to pay particular attention to hypertension, in its various aspects; and when these institutes make their own more detailed plans the research-workers will choose investigations which they themselves want to pursue. "Planning does not mean that if a worker is interested in something else he can't do it. He can."

THE OUTLOOK

Some of the institutes we visited were splendidly equipped, and their staff were clearly of high quality. But I cannot believe that they will play their full part in the development of medicine until their research-workers are able to work without looking over their shoulders. The very essence of science is that facts are facts, whoever discovers them; and Russian investigators will remain under a grave handicap so long as those who accept Western discoveries or ideas know that they are liable to censure as "lackeys of bourgeois science" or worse. The Soviet Union, like the rest of us, will sooner or later have to choose between science and chauvinism.

Anyone who values the international medical tradition, which for many centuries has been one of the integrating influences for mankind, must welcome the new policy by which foreign doctors have again been invited to see what is being done in Russia, and they must be even more glad to see Russian doctors returning as visitors to our own medical institutions and to international conferences. What is now required, however, is not so much the exchange of further "delegations" as the exchange of research-workers and other experts who can spend some months in each others' countries both in learning and in teaching. To exchange journals and translate books is better than nothing, but it is a poor substitute for personal contact between people who are doing similar work.[27]

Meanwhile, if the U.S.S.R. wishes to give further proof of her desire to coöperate in the tasks of medicine, none could be more encouraging than her resumption of membership of the World Health Organisation, which is so much concerned with the wider dissemination of knowledge and techniques.

V. SOVIET MAN

Viewed as a means of preventing and treating disease among vast populations which previously had little or no medical care, the Soviet health services are a very great achievement. That they have shortcomings is freely admitted by the ministry of health itself, but in many respects they are a triumphant demonstration of what can be done by medical skill and devotion. There have been, and are, a great many doctors in Russia whom we should all recognise as people of the finest sort.

The extent to which the population of the U.S.S.R. have benefited physically by these services cannot be summed up in statistical terms, because the vital statistics of fifty years ago are sketchy, while those of today were not supplied to us. The only figure I can offer, which was given to one of our party, is the expectation of life (at birth) of the Soviet citizen, which was said to be just under 50 years.

But the length of life is in any case less important than what one does with it, and I shall conclude with a few rash words on what the citizen appears to be doing and thinking.

THE ENVIRONMENT

A traveller sees chiefly what he expects to see. So I shall concentrate on what, to me, was unexpected:

24. See Crome, L. *S.C.R. Soviet Medical Bulletin*, June, 1954, p. 15. Apter, I. M. *Ibid*, September, 1954, p. 29.
25. Evidence of this change of attitude is given by Harrison E. Salisbury, lately a Moscow correspondent of the *New York Times*, who writes of efforts now being made to persuade Russian intellectuals to discuss and disagree on questions of art and science. *New York Times*, international edition, Sept. 19, 1954, p. 3.
26. The Academy of Medical Sciences, founded ten years ago, is more or less equivalent to a combination of the Royal Colleges with the Medical Research Council. With (I think) only 100 active members and 150 corresponding members, it is relatively small and select; but it has no fewer than 30 research institutes of its own.
27. Foreign medical textbooks are sometimes translated into Russian and published by the ministry of health, without regard to copyright—pro bono publico. When one of us asked whether it would not be useful if Russian journals printed English summaries of their articles, the answer was "yes"; and it would be useful if English journals published similar summaries in Russian."

1. The increasing *approximation* of our ways of life.

While the Western nations are far more socialised than in the 1930s, the Russians for their part are now allowed to buy their houses, invest their money at interest, and leave their property to whomsoever they wish. (Nor did I hear any mention of death duties.)

2. The *efficiency* attained by a nation once thought constitutionally incapable of using machines.

Red tape, waste, poverty, and misery there doubtless are: but Moscow, with its vast clean streets, its increasing traffic, and its superb ballet, its opera, and its music, is emphatically one of the world's modern capitals, profoundly impressive to its many visitors from the East. Like Russian transport, on land and in the air, it works.

3. The *material progress.*

Over much of the countryside the roads are just earth tracks, and a few hundred yards from our luxurious hotel in Moscow was a picturesque slum area of wooden houses no doubt grossly overcrowded. But Russia, as they told us, is a land of great contrasts and rapid changes; and the citizen—provided he likes huge blocks of flats, and skyscrapers that look like Gothic cathedrals on the skyline—has ample reason to think that things are on the move. Moreover, though much of what goes up is of "utility" grade or lower, the Soviet authorities have always been so wise as to make just a few of their new structures the finest their architects could devise.

Long notable among these symbols of a new and possibly better world is the Moscow Metro, whose underground stations—all different and some of them really lovely—grow more fabulous with each extension of the lines. More recently the citizen has been inspired by the astonishing new home of Moscow University, with its central tower of 25 storeys, its immense marble vestibules, its graduation hall with 1700 seats, its 35 lecture-theatres, its laboratories, its shops, its swimming-bath, its gymnasium, its policlinic employing 28 doctors (mostly whole-time), and finally its living accommodation for some 6000 of the students and staff. By a tremendous effort, all this was put up in three years, complete from the refrigerators in the students' kitchen to the sculptured faces of humanity's greatest thinkers; and, though it is not at all my own idea of a university, I cannot help wishing that we in this country more often felt that we too could afford some extravagant symbol of confidence in our future.

Of course, Moscow is the capital; but, when told that we had only been to Leningrad, Moscow, and Georgia, two air-pilots remarked: "Coo, you've seen nothing yet. You should come back with us to Siberia." Nor did they mean what they might have meant. They were thinking perhaps that what is really exciting in Russia is not the city buildings but the colossal engineering projects in which rivers are diverted and connected, mountains are razed, and new seas are to be created—with climatic changes to follow.[28]

4. The *Victorian* parallel.

As in Britain last century, the new ability to make things on a large scale has enabled the Russians to express themselves in quantities of mass-produced decoration—in concrete, plaster, plush, and plastic. Having abandoned the functional styles of the 1930s, their architects are feeling their way to a new one; but the stylistically conglomerate buildings they are now producing, though they sometimes look noble in the mass, struck me as generally belonging to the 19th century rather than the 21st. Similarly, pictures, sculpture, and theatre scenery are all severely representational; and we found it hard to explain Henry Moore to critics who were quite sure that the test of art is that it should appeal to the many not the few.

No doubt this attitude is the reason why in Russia one so seldom catches the breath and says "That's original—that's new." The Moscow Agricultural Exhibition, especially when floodlit, is far more beautiful than our Festival was, but distinctly less sophisticated and amusing.

THE PEOPLE

Having noted similarities between the cultural life of Soviet Russia and the cultural life of Victorian Britain—both of them countries in a productive phase following an industrial revolution—one is tempted to think it more than fortuitous that the Russians, like the Victorians, seem so very respectable. At the ballet, at the seaside, and even in the Dynamo stadium, their behaviour is decorous, their manner rather grave, their clothes tidily inconspicuous. They are enjoying themselves, but without giggles or bursts of raucous laughter, and indeed much laughter at all.

How far this emotional sobriety is due to natura causes, and how far to Communist insistence on good manners in public, I have no idea. But the Party must be at least partly responsible for the absence in young Russians of that conspicuous preoccupation with sex which in other countries is so often induced by books, newspapers, comics, advertisements, and entertainments. To listen to a music-hall show in which there seemed to be no risky jokes whatever made one feel that the local culture was not so much Victorian as Puritan. And the psychiatrists tell us, of course, that Puritanism has its own dangers.

The Russian child is separated from his mother for considerable parts of nearly every day, but he is early inured to social life with its sanctions and its own emotional satisfactions. Can the Russians be right when they tell us that neuroses and other psychological disturbances are uncommon among the men and women brought up in this way? Outside observers have pointed out that, in a society where so much is laid down in black and white and accepted by the child without question, there is far less room for conflict and anxiety; and care-free happiness is likely so long as one is accepted by the group. To those who believe and belong, the Soviet experiment is the grandest thing in the world, enlisting their altruistic effort; and, in shutting their eyes to so much, they can ignore even the price that has been paid for it in the sufferings of millions of their compatriots. But, as the years go by, the faith of adults cannot be indefinitely maintained by repetition of old sayings, unless these embody great truths; so it is significant to read that under the new régime there is now "a tendency to subordinate ideology to common sense, an effort to put some moral content back into trite party shibboleths."[25]

"DON'T PASS BY"

In a country of compelling slogans the one I liked best is the newest, and perhaps the oldest. It was explained to us something like this:

"In our schools, you see, the clever children and the less clever ones work all together in the same class. That is all right, because when the clever ones have finished their task they can help the others. Together the children form a collective, a community, and they all learn together. The same applies when we've grown up; and this saying "Don't pass by" means that whenever we see anything wrong we should say to ourselves: 'I am the member of the collective who is here on the spot—the representative of the community. So I must not pass by but must do what I can.' When I see someone in trouble or danger I must say: 'This is a Soviet man; I must help him.' . . . Indeed I must help any man."

The last words were an afterthought perhaps; but they carry our hope for the future.

Like all the members of our party, I am very grateful to our Soviet colleagues who spent so much time in showing and describing their work and to those who entertained us in their homes. The staff of the ministry of health of the U.S.S.R., whose hospitality we enjoyed, and of the Georgian ministry of health, were indefatigable in their help, and we are happy to remember much kindness from them and from many others who attended to our innumerable wants. Our interpreters suffered most, but are cherished most warmly in our memories of the expedition.

28. *Manchester Guardian*, Oct. 4, 1954, p. 1.

Public Health

THE INTEGRATION OF HOSPITAL AND COMMUNITY

I. GORDON
M.D. Edin., M.R.C.P., D.P.H.
MEDICAL OFFICER OF HEALTH, ILFORD

SINCE the start of the National Health Service in 1948 there have been two important changes in the hospital service. The treatment of patients in hospital has improved, and the relation of the hospitals to other branches of the health service and to the communities they serve has deteriorated. The improvement in treatment costs the nation vast sums; while improvement in coöperation would cost little, and yield information at least as important as that obtained in the laboratory.

Before 1948 many general hospitals, most maternity hospitals, and nearly all fever and mental hospitals and sanatoria were controlled by local authorities, and the doctors on their staffs had to maintain some liaison with the community. After 1948 this control disappeared. Today most of the doctors who work in hospitals and who advise their lay committees and administrators recognise no obligation save to treat the patients in the ward or outpatient department and develop their own unit. Some enlightened specialists take some cognisance of the needs of their patients before they come into hospital, their social circumstances when they are in, and their needs after they leave,[1] but by obligations to the community I mean something wider than this. I refer to the needs of all the sick and potentially sick outside the hospital walls, and the need for coöperation with those who care for them.

The misconception, by medical officers of health and hospital doctors alike, that health can be considered apart from disease, has led to legislation, and an attitude of mind, which assumes that the sick are the responsibility of the regional hospital boards, and the healthy of the local health authorities. Accordingly the responsibility for large numbers of the population—such as the aged and the convalescent—cannot be fairly placed on either authority. Finally, it must be conceded that many a hospital has no defined community (and its officers) with which to coöperate.

Coöperation between People

Lack of understanding of social medicine among specialists (except psychiatrists) cannot be attributed to the National Health Service Act, but the Act did not make things any better. The sessional scheme, especially in the Greater London area, whereby part-time specialists rush from one clinical session to another in a different part of London, and live in yet another area, is not conducive to social and local interests. It costs the country vast sums in travelling expenses, and is one of the reasons why patients are kept waiting in outpatient departments. Local voluntary organisations rarely have the help of hospital doctors, although general practitioners, just as busy, do help. In appointing a specialist to a local-outpatient clinic a board is apt to pay more attention to a candidate's teaching-hospital connections than to his local connections, including access to beds.

Up till 1948 all the local-authority doctors in Ilford worked in hospital wards as well as in clinics. Now, despite a ministerial circular [2] recommending employment of local-authority doctors in hospitals, none do, and the boards have appointed, and pay, full-time physicians to do this work; which is one of the reasons why the health-service costs have risen. Yet, doctors in the public-health services could surely appropriately share in the work of the fever, maternity, tuberculosis, geriatric, and pædiatric wards.

Again, health visitors are employed by local authorities to visit patients in their homes. Hospitals have almoners who, if there were enough of them, and if some had their way, would duplicate the work of the health visitors. There should be no conflict between the almoner and the health visitor. The almoner can supply technical help to the patient, as directed by the hospital doctors, the health visitor has a comprehensive social knowledge of all in her district, and is their continual friend and adviser. The almoner should contact the ex-patient or patient-to-be through the health visitor. The health visitor should be welcomed in hospitals and should have contact with hospital staff, for she can take much useful information there and bring much thence to the general practitioner and public-health department.

Hospitals should also coöperate with the local authority to obtain the services of district nurses and home helps on the discharge of their patients. Maybe one day the average (the exceptional does so already) fever consultant will realise that a highly skilled officer—the sanitary inspector—does visit the home of the patient admitted for suspected food-poisoning, and can give him helpful information.

All these people—school physicians, maternity and child-welfare physicians, health visitors, sanitary inspectors, district nurses, home helps—are employed in groups by a local authority. If hospital areas were contiguous with the same groups much of the present confusion could be less confounded.

Sharing Premises and Information

Outpatient accommodation in hospitals is often grossly inadequate. Some local-authority clinics are housed in premises more modern than the hospital accommodation. Yet there is a school of thought that would transfer all specialist clinics from local-authority premises to the hospitals, on the ground that at the hospital technical facilities are at hand. But at the local-authority clinic the equally important social information is more likely to be available, the clinic is probably nearer the patient's home, overcrowding is less and waiting-lists shorter, appointment systems may work more smoothly, and children are more likely to feel at ease. The specialist often is the same whether the session is held at the hospital or the local-authority clinic.

A health service cannot function without adequate information. Some of this information is required by Act and regulations, but much of it is inadequate for dependable action. The types of diseases now notifiable do not include all that require community action (such as Weil's disease and trichinosis) and include others (such as erysipelas and relapsing-fever) that are now of no interest to the medical officer of health. The information is late because it comes by post, often addressed to the wrong M.O.H., and forms may be delayed and signed in batches. Formal notification is no alternative to discussions by telephone or personal visits. The hospital doctor, and of course also the general practitioner, should know which M.O.H. to contact and, better still, know him personally; and they must know what kind of information is wanted. The M.O.H. must likewise know the doctors and the hospitals in his area—and not only the isolation hospitals. If there is an outbreak of trichinosis, how is an M.O.H. to find out how many cases there really are without warning doctors in general hospitals where cases might be admitted?

1. Lane, R. E., Goodman, N., Saunders, M. P. *Lancet*, 1954, i, 1229.
2. Ministry of Health circular 118/47.

The hospital specialist in his turn may find useful the school-health-service and child-welfare records. In a town such as Ilford there are notes, some very comprehensive, of all the 23,000 school-children and 12,000 under-fives. Many include hospital notes which are probably not otherwise available when the child visits yet another hospital. A minor victory is to persuade a somewhat aloof and suspicious hospital physician to appreciate such dossiers, and even, by persistence, to get him to ask for them. Few specialists object to receiving medical information about their patients, but many object to giving it—though surely there can be no ethical objection to giving information about school-children to the medical staff of the local education authority, who must by law arrange for their medical examination. Many hospitals do of course send the M.O.H. discharge-notes for their children. But in some the specialists are content to benefit by the notes of others, and do not help in their turn by passing on their own information.

Apart from these general opportunities the special services of the local authorities and the special departments of the hospitals offer useful opportunities for coöperation.

Specialised Services

Pædiatrics

The local authority has a statutory obligation to provide child-welfare services and a school-health service. In some areas, especially that of the London County Council where there are children's hospitals with forward-looking consultants, there is already considerable coöperation between the two services. Local-authority physicians work in hospital wards, and pædiatricians take a part in the school-health services and infant-welfare clinics; but on the periphery the specialists tend to be more aloof and suspicious.

Geriatrics

Hospitals and local authorities should coöperate closely in this service because it is often impossible to decide who should care for an aged person too ill for a hostel and too well for a hospital bed, and because all efforts should be made to provide medical attention for old people at home among familiar faces and surroundings. Whether an aged person is to be admitted to hospital is a social as well as a medical problem, and full details of home conditions can be given to the admitting officer by the local authority. Before old people leave hospital some investigation should be made of the home, if any, that they are going to.

Tuberculosis

Since the tuberculosis services left the control of the local authorities in 1948 owing to the development of modern treatment the mortality-rate has fallen; but the notification-rate shows little change, and the names on the tuberculosis registers are increasing. Many who otherwise would be dead, or confined to bed in hospital or at home, are now ambulant members of the community, and are thus potential spreaders of the disease. The importance of searching for the source of infection and examining contacts has, if anything, increased.

Coöperation between the local authority and the chest physician continues, for their areas usually correspond. The local authority pays part of the salary of the chest physician and provides him with his tuberculosis visitors, occupational therapists, and home helps and with open-air shelters and free milk for domiciliary cases. The local authority pays for convalescence, and maintenance at the residential homes, and arranges the funds of the aftercare committees. Both may carry out B.C.G. vaccination. The chest physician notifies the M.O.H. of cases of tuberculosis, the M.O.H. informs the chest physician of notifications from other sources. The M.O.H. keeps a register (not by obligation now) which, if carefully supervised, is a better indication of the cases of tuberculosis in his area than the list at the chest clinic, which may merely become a record of current cases under observation and treatment. The chest physician must coöperate with the school-health service in tracing contacts and sources of tuberculosis in the schools. He must coöperate closely with the M.O.H. and housing authority about families that would benefit by rehousing, and with the M.O.H. in arranging employment of the tuberculous. The hospital service provides miniature mass radiography; the local authority must advise on its deployment.

Since the sanatoria left the control of the local authorities liaison has slackened. In Ilford, of 40 discharges from sanatoria in the first half of 1954, we have been notified of only 29. Yet homes are often overcrowded and unsuitable, and susceptible children may live there. At least preliminary notice should be given to the local authority. Sanatoria of course are interested in admitting the treatable patient who will respond to treatment, local authorities in the patient who will spread infection.

Infectious Diseases

Isolation hospitals were nearly all built, administered, and staffed by local authorities for community purposes, and as a result coöperation with the local authorities was excellent; these hospitals were exempted from the need to notify cases of infectious diseases as the M.O.H. managed them. In 1948 they were transferred to the boards, many assistant medical officers became consultants, and the community obligations of the hospital became subordinated to the clinical interests of the new directors; but the law with respect to notifications has not been changed. Before 1948 many of the largest authorities had full-time specialists in infectious diseases; elsewhere the M.O.H. did the clinical work himself. Some M.O.H.s never entered a fever hospital, and acted on notes of the admissions and formal notifications; others followed the day-to-day conditions of the patients and arranged community preventive measures accordingly. These two classes still exist, with a third—M.O.H.s who formerly managed fever hospitals but now must depend for their information on a consultant. An M.O.H. must have day-to-day access to a fever hospital to obtain up-to-date information about patients if he is to perform his duties to the community adequately. Cases are often not fully diagnosable on admission; and diagnoses may change. Much has rightly been said about general practitioners visiting their patients in hospital, but there is little he can do at that time. It is even more important that the M.O.H. should visit the fever hospital, for he must decide what preventive measures are necessary for the community while the patient is still in the ward.

Should the M.O.H., then, have clinical control of fever hospitals? I doubt whether it is possible for a M.O.H. today to control enough beds to obtain adequate experience in the modern treatment of, say, poliomyelitis and tuberculous meningitis, and still have time to be the community physician of a reasonably sized area. The M.O.H., however, should have some say in the policy of the infectious-disease wards. Because a disease, such as scarlet fever, is notifiable, that does not in these days imply that cases should be nursed in hospital unless the home circumstances require it. Because a patient has symptoms that resemble an infectious notifiable disease, such as dysentery, food-poisoning, meningitis, or typhoid, it is not necessary that the fever beds should be cluttered up with odd cases of diarrhœa, vomiting, headaches, or pyrexia of unknown origin—the symptoms of half the patients in a general hospital. If there are not enough true cases of infectious diseases to fill these beds they should not be used for sham infectious fevers, but transferred to other specialties.

A fever hospital should have a defined catchment area, not too large; and it should be within this area. Then the patient with, say, poliomyelitis has not a long journey by ambulance, and visiting by relatives is easier, especially for parents of young children. The admission officer knows his general practitioners, and thus knows which give a reliable diagnosis and which are likely to try to "pull a fast one"; it is easier for the consultant to settle a difficult case by domiciliary visits; and the M.O.H. can visit the hospital regularly. I suggest that

each fever hospital should have as its catchment area a metropolitan borough, county borough, or county district, or a group of these. In an emergency cases might be accepted from local authorities which immediately bound the catchment area. There should be a special relation between the fever hospital and the metropolitan borough, county borough, or county district in which it lies. The M.O.H. of such is responsible for the health of the sanitary area he supervises and should at all times know what infectious cases are in the fever hospital. In Ilford each morning the fever hospital gives by telephone a list of all the previous day's admissions, irrespective of their domicile, to the local public-health offices. Medical officers of health of other areas are then immediately notified by telephone of admissions from their own areas.

Mental Health

Officers of the local health authority are responsible for initiating steps for the admission of cases to mental hospitals and the aftercare of patients after discharge. In many areas, where psychiatrists and psychiatric social workers are employed jointly, there is a close link between the staffs of the two authorities. In other areas, mainly in large amorphous counties, the connection is of the loosest; the hospital may have a catchment area which is only part of that of a local-health-authority officer, or not in it at all.

Mental hospitals usually have defined catchment areas. These should correspond to those of county boroughs, metropolitan boroughs, or county districts, or groups of them. They should be as near to their catchment areas as possible, so that patients may return to their communities temporarily or permanently as soon as possible, so that relatives may visit and not lose contact, and so that the mental-hospital staff may take some place in outside work—if possible in outpatient clinics, child-guidance clinics, clubs for aftercare, and domiciliary visiting.

Contact with the mother and home is also helpful for mentally defective children who are in hospital. Support by experienced workers may help the mother who has to care for these children at home, and may even make it possible to keep a child at home who would otherwise fill an institutional place. Links with the community may help in the employment and resettlement of the feeble-minded.[3]

The local authority must of course ascertain the mental defectives and pass them to the hospital for institutional admission. Again there is opportunity for misunderstanding about priorities, especially as the local authority must supervise any patient not admitted because of the severe shortage of institutional accommodation.

Obstetrics

A proportion of births, which varies from area to area, is domiciliary. Selection is required, and it is generally accepted that the decision as to where the confinement will take place should rest on medical and social grounds. A Ministry circular [4] has stated that the M.O.H. of the local health area should be consulted on the social aspects of the case. Unfortunately, as with many another Ministerial circular, in many areas little notice is taken of it. Mothers are often booked in order of application; the general practitioner makes a successful direct approach to a specialist for his own cases irrespective of their needs; and the small proportion of beds that may be kept for special cases is soon exhausted. The result is that there is a scramble, and patients who need accommodation on social grounds do not get it, or have to go far afield.

Arrangements for antenatal examinations may be chaotic, especially if the mother lives at some distance from the hospital for which she has booked. The hospital may provide an antenatal service, or may arrange for a local authority to do so; or the general practitioner may make the examination. As a result this work may not be done at all, except perhaps for a visit at about the 36th week, or it may be done twice over, at double expense to the State.

Difficult domiciliary confinements and difficult babies may need the help of obstetrician, pædiatrician, or hospital. Flying-squads or premature-baby units, and the training of midwives in domiciliary work, offer obvious opportunities for coöperation between local authority and hospital.

When the mother and child leave hospital and the health visitor takes over she will want to know when the pair are to be discharged and any directions about feeding and management. All this would be enormously simplified if each maternity hospital had its defined catchment area consisting of a local authority or group of such; each set of officers would know exactly with whom to coöperate.

Other Services

Local authorities provide ambulances, hospitals use them. A Civil Defence Corps is organised by the local authority, and in war it must deploy the mobile units provided by the hospital service; in peace the latter may well use the trained C.D. personnel in disasters. Hospitals provide convalescence for the sick, local authorities recuperative holidays for those not requiring medical and nursing attention. Both supply appliances and sick-room equipment. Regional boards may use and inspect private nursing-homes licensed and inspected by local authorities. In all these fields there may be coöperation, or frustration from the lack of it.

Areas of Coöperation

If a hospital is to coöperate with a local authority it should feel some community with that authority. The authority, in its turn, should think of the hospital as "ours"; and the staff of each, medical and lay, should know one another well and work together.

When the regional hospital boards divided their areas into those of hospital management committees, a happy chopping took place by which, especially in the conurbations, scant respect was paid to communities; and employees of the boards, with a gleam of righteous fervour in their eyes, declared that in their work they took no notice of local-authority boundaries. Soon they found that their catchment areas were not indefinitely expansible, and arbitrary limits arose, convenient to themselves and nobody else. Pending local government reorganisation, local-authority boundaries are not all that they should be, but, at the moment, they are the only available administrative definition of communities and a multitude of services provided for them.

To have every hospital group conterminous with a local authority is a counsel of perfection; but, according to the type of hospital, joint grouping by local-authority area or areas should be possible. This simple alteration would obviate much human misery and official frustration.

But what kind of a local authority? The moderately sized county boroughs employ a M.O.H. who himself knows the authority area and does not distantly supervise area medical officers; who knows the general practitioners, specialists, hospitals, nursing-homes, and hospital doctors, and who deploys all the medical or auxiliary personnel. Pending a reorganisation which will divide all the country into areas of this size, with populations of 50,000–250,000 (which I would call a primary local authority), I would suggest that hospital groups should be conterminous with metropolitan boroughs, county boroughs, and county districts, or groups of them. Some M.O.H.s suggest that the country should be arbitrarily broken down into units of 1 million population for local government and hospital administration. Geography, community sentiment, economics, tradition, transport, the need for local interest, and demands of regional coördination would all militate against such an artificial solution.

Each M.O.H. should sit ex officio on the hospital management committee of his group. He will only

3. Hilliard, L. T. *Brit. med. J.* 1954, i, 1372.
4. R.H.B.(51)74.

occasionally be an employee of the hospital, so little objection can be raised on that score. At present the M.O.H. of one area is often on the management committee of another area, perhaps to make sure that he will not disturb the committee with local comprehensive knowledge. Some sort of association of hospital groups in a larger body, comparable to the present regions, which would correspond to a larger number of local authorities would also be advantageous.

The present system of interlocking memberships of hospital management committees, executive councils, and local authorities means that the same people see each other pretty often; but the man who has the information and the executive power is rarely in the place where he is needed. The lawyer, farmer, shopkeeper, and bank clerk who give their spare time to this work may live in one district of an enormous county, such as London or Middlesex. They go from county-council health committee to executive council to hospital management committee, and if they are able they have a grasp of general policy; but they cannot help much in detailed coördination—for this an officer such as the M.O.H. must be present when decisions are made. Apart from the M.O.H. the local authority must have firm representation in the hospital management committee. There is much loose talk about the freedom from politics of nominated bodies, as compared with elected bodies. Actually a large proportion of lay members on hospital management committees are there, in the final analysis, because they belong to a political party, however public-spirited they are. The local authority has a moral advantage in that elected political minorities have statutory rights of membership.

Coördination by committees of representatives of different interests of the medical services has been considered by regional boards on the recommendation of the Central Health Services Council.[5] A colossus such as the North East Metropolitan Hospital Board would have to consult the following: 27 hospital management committees, 4 county councils, 3 county boroughs, a large number of county districts, several teaching hospitals, executive councils, local medical, dental, and pharmaceutical committees, and the University of London. Probably nothing has come of this scheme, because local areas for different services do not correspond, and other services are not locally managed. Clearly coördination between hospitals and local authorities cannot be achieved by circulars from the Ministry of Health.

Conclusion

Since the National Health Service was introduced in 1948 treatment of patients in hospital has improved, but the relations between hospitals and communities have deteriorated. The reasons for this deterioration are that most hospital doctors do not appreciate their obligations to the community; and there is a statutory, and incorrect, presumption that the public can be divided into the sick, who are cared for by the hospital services, and the healthy, who are the responsibility of the local authorities.

Potential points of contact between the hospital and the community are the other health and social services of the area and the staff who run them.

To remedy this lack of coördination it is suggested that the areas of hospital management committees should correspond to local-authority areas, and that local-authority officers and members should be adequately represented on the hospital committees. This arrangement does not exclude the association of the hospital groups in a regional organisation.

5. Central Health Services Council. Report on Coöperation between Hospital, Local Authority, and General Practitioner Services. H.M. Stationery Office, 1952.

RECEPTION CENTRE

WHILE "that child is best served by a reception home who never gets into it," as Mr. Kenneth Brill[1] wrote a few months ago, for the child who does get in (as his own experience in Devon has shown) the reception home provides a unique service. The result of the Mersham experiment, the report of which by Dr. Hilda Lewis[2] has just appeared, underlines the same conclusion.

The proposal that the Nuffield Foundation should finance a pilot experiment in the reception, investigation, and disposal of deprived children was made by the council of the Caldecott Community in 1944, at the instigation of Miss Leila Rendal, its director; and the community, with its long experience in the care of deprived children, was asked by the foundation to sponsor the study.

The report covers the years between October, 1947, and July, 1950, when the centre was transferred to the Kent County Council. The findings have not been published until it was possible to include the results of a two-year follow-up inquiry on 240 of the children.

The centre received the most difficult children, with the most unfortunate backgrounds, which the county could produce. The proportion of their families in the lowest social class was higher than in the general population, and 30% of them were living in overcrowded rooms. In many cases the parents were dead, unknown, or out of reach, and among the parents who were living together relationships were harmonious in only 10%, tolerable in 45%, and bad in 45%. "Cruelty, drunkenness, crime, indifference to their children, and sexual laxity were noted in some of the parents." In 279 of the 363 families concerned there was some mental disability in one of the parents—defects of intellect or personality, or definite mental illness. Some 63% of the children had been separated from their mothers as a result of war-time evacuation or for other cause, and in 28% the separation had lasted several years. Over half the children were committed by the courts to the care of a fit person—200 before they reached the centre, and 75 afterwards, on the centre's recommendation.

They ranged in age from 5 to over 15 years. Children under 5 were taken only if they belonged to a family of siblings whom it was undesirable to part. The children remained in the centre for only a few weeks, being reassured and properly nourished, and told what was being arranged for them and why. Dr. Lewis, as psychiatrist to the centre, was able to observe their day-to-day behaviour as they settled down, and to test their intelligence in a favourable atmosphere. The warden and her staff, too, reported on the physical and emotional needs of the children. On admission nearly 40% showed neurotic symptoms, and 32% were delinquent; some 47% were of normal intelligence, and 28% had an intelligence quotient of less than 90, and 23% above 110. Their chief symptoms before admission were anxiety, enuresis, pilfering, and wandering.

When all observations had been made and records of past history and social background assembled, the child's future was reviewed at a conference attended by Dr. Lewis, Miss Rendal, the staff of the centre, the welfare officers and probation officers who had had dealings with the child's family, the children's officer for Kent, and sometimes a magistrate. For children who had already been committed to the care of a fit person, placement—or replacement—with their own parents was not a practical proposition; and there were many others whose homes were judged to be too bad for them to return to. Such bad homes, it has often been noticed, are not necessarily devoid of affection; and Dr. Lewis mentions, in passing, that

"... after a period at Mersham on remand, a child would be brought before a juvenile court at which his parents, who had

1. *Case Conference*, May, 1954, p. 12; see *Lancet*, 1954, i, 1336.
2. *Deprived Children*. London: published for the Nuffield Foundation by Oxford University Press. 1954. Pp. 163. 9*s*. 6*d*.

proved incapable of bringing him up properly, would display their resentment or distress at being parted from the child; when the child was then perhaps sent straightaway to a children's home or hostel he harboured the same feelings of unhappiness and hostility as he had seen in his parents."

She thinks that in such cases it would be better for the child to return to the reception centre for a few days to learn about the reasons for the new arrangement that has been made for him. Certainly if children must endure public and painful separations (which everybody, including the magistrates, tries to avoid), they should at least be taken back for a few days to surroundings which have become familiar. There must be better ways of dealing with this situation, in which retraining of parents could sometimes have a prominent part. Evidently we have here a serious gap in our welfare services.

Only about a fifth of the children were recommended for foster-home care. Dr. Lewis, indeed, draws attention to some disadvantages of foster-homes which are apt to be overlooked. Thus few foster-parents, she finds, will tolerate or favour continuing contact between a child and his real parents; and again, some foster-parents judge a child severely for faults which they would regard leniently in a son or daughter of their own. Rejection, and repeated rejection, may then be the lot of the child; and nothing is more destructive. He may become incapable after a time of showing affection: but the truly "affectionless" child, she finds, is rare—even among those who have been long separated from their mothers. "Reserved, unattractive, outwardly cold, children may convey a spurious impression that they cannot give affection and do not want it from others; but this protective façade frequently hides a longing for affection. . . ." Such apparently irresponsive children need exceptionally gifted foster-mothers, and these of course are rare. Slightly more than a third of the children were recommended to children's homes; other types of placement were to boarding-schools, schools for the educationally subnormal or the maladjusted, or approved schools.

The value of reception centres is that they give time and opportunity for the careful and considered placement of deprived children coming under care. Three-quarters of the children in this experiment were placed in accordance with the recommendations of the Mersham centre; and of the 240 followed up after two years, 63% had improved in varying degrees, 29% had not changed, and 8% were worse. The portion in good psychological and social state had more than doubled since they had left the centre; and children placed according to the recommendations made by the centre had fared somewhat better than those not so placed. Other findings were in line with these, suggesting strongly that this reception centre, at all events, had played a key part in restoring many children to a normal course of development.

Medicine and the Law

DEFENCE OF DOCTOR AND DENTIST

THE two English medical defence societies have lately held their annual meetings. The Medical Defence Union has its offices at Tavistock House South, Tavistock Square, London, W.C.1, and the Medical Protection Society at Victory House, Leicester Square, W.C.2.

Medical Defence Union

Presiding over the 68th annual general meeting on Sept. 21, Dr. S. COCHRANE SHANKS, the president, said that the year had brought no abatement in the flood of medical litigation, nor any reduction in the large sums awarded as damages. In about 80% of the cases brought against doctors, the plaintiff was assisted under the Legal Aid scheme. He cited two cases, both successfully defended by the Union, where the costs of defence were £7700 and £2600, none of which was recoverable from the plaintiffs, who were assisted persons. He thought that a case could be made out for imposing on a plaintiff or on the scheme a proportionate liability for payment of the costs of a successful defendant.

Figures published by the Ministry of Health showed that sums paid by hospital authorities in compensation of all kinds rose from £7500 in 1948–49 to £153,000 in 1953. Dr. Cochrane Shanks believed that high tide had been reached: "judges, if not juries, are beginning to realise that mishaps can occur in treatment when there is no suspicion of negligence, that there are some risks inherent in all medical and surgical treatment."

During the year an agreement was concluded between the British Medical Association, the defence societies, and the Ministry of Health which had resulted in the Ministry withdrawing its previous instructions to hospitals to join doctors as co-defendants or to seek contribution from them after the event. In future doctors and hospital authorities would not be seen fighting each other in the courts. Damages awarded or settlement out of court would be met in agreed proportions, or, in default of agreement, in equal shares.

In 1953 the membership of the Union rose to 40,837, an increase of nearly 2000 on the previous year. The number of cases handled was 2384; the corresponding figure for 1952 was 2266.

Medical Protection Society

Sir ERNEST ROCK CARLING, in his presidential address on Oct. 6, remarked that doctors, like others, were subject to aberrations, and when it appeared that a mistake might reasonably have been avoided the society accepted the consequences. But that was very different from accepting the view that every mischance of treatment or operation is due to negligence.

"We adhere firmly to the judicially expressed view that even with 'reasonable care and skill'—even in the hands of the meticulously careful and most highly skilled—mishaps and unforseeable accidents are not only possible but, in the nature of our work, now and again inevitable. That position we defend with all our might."

Difficult situations sometimes arose from the use of apparatus potentially dangerous. Which individual, in theatre practice, could be held responsible for the continuing perfection of a complicated piece of electrical apparatus? There might be regular dates for tests, but what if an accident happened the day before that date fell due? Who was responsible for the diathermy pad, its adequate size in relation to the current, its positioning and contact? Theatre routine was ordered with great care and could be relied upon, but, with necessary changes of staff, could not be absolutely and invariably impeccable.

Besides belonging to a protection society—indeed out of proper regard for the interests of fellow-members—doctors and dentists should protect themselves. Sir Ernest again urged the importance of keeping contemporary records, especially of casual patients.

The society was still not wholly satisfied with the working of some of the dental-service arrangements. Dental surgeons should bear in mind the importance of obtaining a written understanding from any National Health Service patient for whom he proposed to do work not provided for under the scheme, and should complete any dental treatment under the N.H.S. before starting further treatment privately arranged with the patient.

In 1953, 1530 new members were elected, bringing the total membership to 28,545. During the year 2020 cases were dealt with.

In England Now

A Running Commentary by Peripatetic Correspondents

WHATEVER nestles inside those rows of gleaming bonnets at the Motor Show may tick over silently and politely on the road, but inside my own bonnet there are three bees that buzz with frustration at the ways of motor-car manufacturers. I do not pretend to understand the technicalities of design, I am only the poor fellow who is fated to spend half his waking days pursuing the elusive bread and butter, wrapped up in a chunk of expensive ironmongery.

In the good old days my motor-car retained the fragrant elegance of a carriage. I could enter it with a proper flourish of professional dignity, turn around inside, and drive away with a courtly doff of my hat. I could see over hedges and walls, bow to familiar faces, and even enjoy the fleeting warmth of the English sunshine. Now my chariot smacks of a soapbox Derby. I have to crouch down in disc-cracking scoliosis, present a back-sided farewell to my patients, and insinuate my corpulent frame into the cavity with an intricate cockpit drill. True, there is no longer a top-hat for my stethoscope; I just flop down on my battered trilby and a pad of certificates. I cannot see round the corners, I am forced to recognise my ambulant patients by their legs, and the roof of the car is sealed with claustrophobic proximity to my cranial vault. In short, we have sunk too close to the gutter.

Motor-car designers must be spartan, celibate men, with strictly urban tastes. Otherwise they would not tantalise the rest of us with luggage-boot lids that hinge at the top. How I sigh for the good old back panel that let down to make a carrier worthy of a two-ton lorry, so that the family could set out for their holidays with mountains of kit and cherished strange-shaped oddments, hard down on the springs; so that I could pop a bale of straw or a sack of potatoes on the back during my country round; so that we could set out the picnic table in comfort; so that I could remove my midder bag from the boot without being clocked on the head by one of those glorified rat-traps. Combinations that button up the back are not nearly such an embarrassment to general practice as a luggage boot that hinges at the top.

And lastly I have to grumble about those fatuous winking lights that have replaced the unmistakable semaphore indicator arms. To alter conditioned reflexes at my time of life is an injustice that makes even Pavlov's dogs turn in their graves, and I too am slow to learn new tricks. The façade of a modern motor-car is beginning to look like Piccadilly Circus at night, and by day that insistent winking is a vulgar assertion of impatience. It is all so confusing that this morning I found myself winking my right eye at the policewoman on the corner. She winked back, but alas I felt too old to go ahead.

* * *

The politically aspiring doctor has an advantage over the politically aspiring layman, as was clearly demonstrated to me during our recent General Election. As my husband's canvasser-in-chief, I was tackling a tough member of our railway community whom I suspected of having strong sympathies with the Native Policy of the Opposition. I brought to bear all my tact, charm, persuasiveness, and sweet reason for the best part of ten minutes.

"You must agree that Doctor B——'s policy is the only possible one for a country such as ours." I ended with my most flashing smile.

"Ought to have shot the lot fifty years ago," was his only reaction. He was indeed a "natural" for the opposition.

"Well, in that case . . ." I said, moving towards the door, "I'll say good evening. Thank you for listening to me so patiently."

"That's all right," he replied with condescension. "Don't mention it. You tell the old Doc he'll have my vote all right. Operated on my piles he did, eleven years ago. Proper corkers they were. Never had a moment's trouble since. Tell him I hope he gets in."

He did, as a matter of fact.

* * *

Monday morning, and I walked into the 10–16-year-old female rheumatism ward for the weekly E.S.R.S. Approaching a row of strict bedders I became aware that something was amiss. I gave myself a furtive once-over, but all seemed to be reasonably normal so I pressed on. The head of the row already had her arm outstretched with her nightdress sleeve expertly knotted to display a venous paradise. The needle sitting pretty, my gaze travelled upwards and met a loop of dirty-looking knotted string suspended from a hole in a red and swollen ear-lobe. Peering round the corner, there was its somewhat eccentrically placed twin. My gaze shifted down the row and ten times was rewarded by the same horribly fascinating sight, the owners all looked remarkably pleased with life. At the end of the row was a 13-year-old with aural appendages as Nature designed them. "Doctor my hand's fair dropping off!" I came out of my reverie and removed the needle.

The normal-eared one was tackled first.

"Are you responsible for this?"

"Yes, doctor, you see we all wanted to wear proper ear-rings when we went home, and as I'd seen it done once I pierced them all in the bathroom last night. We didn't walk at all, we shuffled in on chairs and we cleared up all the mess. You needn't worry that they will turn septic because I used a different needle for each, just like you do."

"What sort of needles did you use?"

"Oh, a packet of assorted darners, doctor."

It later transpired that the ceremony had been witnessed by a junior nurse who saw nothing unusual enough in it to report and who appeared to think it was some customary hospital ritual. She averred that no one had squealed and that there was not overmuch bloodshed. She added, however, that she had thought that the needles ought to be boiled and had offered to do so.

After an attempt at a telling off, the piercer was in tears, but the pierced remained embarrassingly pleased with themselves and quite unmoved by descriptions of impending blood-poisoning. The string "sleepers" were removed and the lobes dabbed with flavine; the smug expressions vanished, but the owners were still dry-eyed and unrepentant. But at the prescription "penicillin three-hourly for three days" their morale broke; the thought of anatomical piercing assumed its true perspective when vanity was no longer at stake.

* * *

Naturally, I hadn't meant to embark on anything like this until much later; but when our $3\frac{1}{2}$-year-old asked me what went "fouf—fouf—fouf" in her ears, and what my heart-beat was—which she happened to hear one day when we were lying on the bed together—I soon found myself involved in the Circulation of the Blood and All That.

The come-back came two months later, when she observed, "I wish I could eat mud like the dicky-birds!" Letting the ornithology pass (for the moment), I asked what purpose this particular feat might serve. "Well, you remember when we were on holiday you told me I had *mud* going round and round inside me mixing up my meat and my vegetables in my tummy and taking them down to my toes?"

* * *

THE MASTER

(September 29th, 1954)

Master, whose fire kindled our glad surprise,
brought tropic seas to drear dissecting room,
so that we heard the thunder and the boom
of surf on reef—and hark, the boobies' cries —
or vitalised some skull, unwound its scroll,
or brought some fossil form to life again,
or thread of nerve in pickled flesh to pain,
you made the living and the dead one whole.
So when we wandered all the earth we sensed
your voice and watched your clear-cut features play,
pausing, perhaps, in moments of that bliss
of finding some rare thing, triumphant, tensed,
seeking to share our joy, then would we say,
"What would I give to hear Wood Jones on this!"

C. G. L.

Letters to the Editor

NOMENCLATURE OF RHEUMATIC DISEASES

SIR,—As you suggest in your leader of Oct. 2, it is time the more accurate term "polyarteritis nodosa" replaced "periarteritis." In their article in the same issue, Dr. Heathfield and Dr. Williams still use the inaccurate term. That the lesions are not perivascular or purely adventitial in distribution was recognised as long ago as 1903, when Ferrari [1] introduced the term "polyarteritis nodosa acuta." Even this term is not strictly accurate as a description of a lesion which involves all coats of the vessel wall (panarteritis), but it does at least indicate the widespread nature of the process. Although the less accurate "periarteritis nodosa" is still extensively used in the American literature, most British textbooks of pathology or medicine use "polyarteritis nodosa."

Is it not time, too, that the nomenclature of certain other rheumatic diseases was revised? The term "rheumatoid arthritis" focuses attention entirely upon the joints of patients whose condition frequently affects the heart, blood-vessels, serous cavities, spleen, lymph-nodes, muscles, nerves, and subcutaneous tissue. Active lesions may be found in one or more of these situations long after the joint changes have become quiescent or "burnt out." Surely, the term "rheumatoid disease," already used by occasional authors, is a more accurate description until the ætiology of the condition is elucidated. It is to be hoped that the American practice of including ankylosing spondylitis as a variant of rheumatoid disease ("rheumatoid spondylitis") will not spread to this country. Despite resemblances the two conditions show many dissimilarities. Likewise "osteo-arthritis" means inflammation of bone and joint—circumstances which apply to practically every non-neoplastic joint disease except that for which the term is used. The term "degenerative joint disease" is used in America and is much more satisfactory for a condition which so often begins as a degenerative change in the matrix of the articular cartilage.

Above all, let us be careful in our use of the term "collagen disease." The work of Klemperer and his colleagues in describing the lesions of systemic lupus erythematosus has been invaluable. But the recent work of this and other groups has shown that collagen and other connective-tissue elements probably play a merely passive rôle as sites of deposition of nucleoprotein. If L.E. cells can be demonstrated, there is no point in retaining the diagnosis "(diffuse) collagen disease" in favour of "systemic lupus erythematosus." [2] There is little justification for calling polyarteritis nodosa "diffuse collagen disease"—a not infrequent occurrence nowadays—for the essential change occurs in the predominantly musculo-elastic tissue of the vessel wall. In rheumatic fever, also, it seems unlikely that the "fibrinoid necrosis" affects collagen itself but rather that ground substance is the site of the abnormality. Indeed, the only "diffuse collagen disease" which essentially affects collagen is diffuse scleroderma. Let us be on our guard then lest the term "collagen disease" outlives its usefulness and becomes a mere label for otherwise undiagnosed conditions.

Medical literature abounds in confusions arising out of the loose use of terminology, and common usage is often the excuse for the continued use of terms which advances in knowledge have rendered inaccurate. Pursuing this argument to its conclusion—that each advance in knowledge should be accompanied by a change in nomenclature—is, of course, a *reductio ad absurdum*. In this instance the terms suggested are descriptive rather than indicative of ætiology, and they cover all the tissue changes discovered as the result of extensive morphological studies. It seems unlikely that any fresh morphological features will be described so that the terms would be satisfactory until the ætiology and pathogenesis of each disease is fully worked out.

1. Ferrari, E. *Beitr. path. Anat.* 1903, **34**, 350.
2. Richards, D. G. *Brit. med. J.* Oct. 2, 1954, p. 777.

Pathology Department,
University of Edinburgh. BRUCE CRUICKSHANK.

PERIPHERAL NEUROPATHY IN POLYARTERITIS NODOSA

SIR,—Localised soft œdema with asymmetrical muscular weakness is a further way in which peripheral neuropathy may present in polyarteritis nodosa. After seeing this clinical picture in a man aged 27, it was possible to make the diagnosis (later confirmed by biopsy) in two other cases in men aged 63 and 58 during the next few months. A large increase in the plasma-albumin was found in the two cases in which this was estimated, but this does not appear a usual finding, judging from the paper by Dr. Heathfield and Dr. Williams. These cases were described [1] in 1944.

Guy's Hospital,
London, S.E.1. RONALD MAC KEITH.

THE EXCRETION OF ALDOSTERONE

SIR,—The administration of aldosterone to 2 patients was described in your issue of Sept. 25 by Prof. Prunty and his colleagues. Advantage was taken of this treatment to obtain some information concerning the excretion and metabolism of aldosterone.

Estimates of the amounts of this steroid in human urine suggest a value of about 0·5 μg. per litre.[2] In view of this low concentration, valuable techniques which can detect it in biological fluids are paper chromatography and bio-assay. Aldosterone in the Bush system of chromatography [3] runs between cortisone and hydrocortisone.[4]

A 24-hour sample of urine, taken while the Addisonian patient received no treatment, was extracted with chloroform (four times $^1/_4$ volume) to remove the free steroids and then by the method of Edwards et al.[5] to extract the steroid conjugates, which were then hydrolysed by calf spleen β-glucuronidase. Chromatography by Bush's system of benzene : 50% methanol = 1 : 1, and development with the combined blue tetrazolium and soda fluorescence technique,[3] showed no free steroids or glucuronides reacting with either reagent.

The urine collected for each of two days while this patient was on aldosterone in a dosage of 400 μg. per day was treated as above ($^3/_4$ of each 24-hour save was used). Development of the chromatographic strips showed no free aldosterone and no metabolites reacting with the developing reagents.

The second patient was a girl of thirteen with the adrenogenital syndrome. Prior to aldosterone therapy, free steroids in her urine, on chromatography, were of the order of 2–3 μg. of free cortisone and no detectable hydrocortisone per 24 hours. Chromatography of hydrolysed glucuronides showed 2–3 μg. of tetrahydro-F, and no other reducing spot.

She was treated with 1050 μg. of aldosterone in divided doses in 24 hours intramuscularly, and then with 750 μg. by continuous intravenous infusion over 24 hours. Half of each 24-hour save of urine was extracted as above. Aldosterone was run as a marker, together with cortisone, hydrocortisone, and corticosterone, each in quantities of 5 μg.

On each of the treatment days, there was a discrete spot on the free steroid chromatogram corresponding to aldosterone. It reduced blue tetrazolium and gave the soda fluorescence reaction of Δ^4 3-ketones. Its R_F value was 0·50 when that of cortisone on the same strip was 0·54. On the standard strip the R_F values were: hydrocortisone 0·40, aldosterone 0·52, and cortisone 0·59. (Aldosterone added to urine runs closer to cortisone than when the free steroids are applied directly to the paper.) The amount of this free aldosterone was about 6–8 μg. per 24 hours, irrespective of the route of administration.

1. *Brit. med. J.* 1944, i, 139.
2. Luetscher, J. A. jun., Johnson, B. B. *Amer. J. Med.* 1953, **15**, 417.
3. Bush, I. *Biochem. J.* 1952, **50**, 370.
4. Simpson, S. A., Tait, J. F. Memoirs of the Society for Endocrinology, no. 2. London, 1953.
5. Edwards, R. W. H., Kellie, A. E., Wade, A. P. *Ibid.*

When the chromatograms of conjugates split by β-glucuronidase were developed, only the spot of tetrahydro-F was apparent on each and in about the same concentration as on the no-treatment days—viz., about 2 μg. per 24 hours.

When aldosterone and cortisone (10 μg. each) were added to 500 ml. of urine of another patient with only trace amounts of free steroids present and subjected to the same extraction and chromatographic procedure, the amounts on the strip were estimated at about 30% of the added steroids.

The use of urines from patients who normally have very low adrenocortical steroids gives one the best opportunities of studying the excretion of free aldosterone and its possible metabolites after the hormone has been administered. The very small amounts excreted in the free state (about 0·8% of the injected dose was recovered) and the fact that no metabolite was detectable which retained its reducing side-chain or its Δ^4 3-ketone, makes it difficult to assess variations in the secretion of aldosterone in various diseases. Although the doses administered were small the amount of free aldosterone in the urine is higher than that reported for normal people and this dose may, therefore, exceed the physiological secretion-rate.

In chloroform extracts of *normal* human urine run by the Bush system, the amounts of free cortisone are usually so great that they extend to mask the presence of the minute quantities of free aldosterone. Increased amounts of aldosterone might show up as a separate spot. By bio-assay an overall estimate of sodium-retaining substances can be obtained, but an assay of aldosterone is only possible if the urine extract is previously chromatographed and the appropriate region eluted as has been done by Luetscher and Johnson.[6]

By paper chromatography, aldosterone can only be detected with certainty in 24-hour urine collections in patients whose adrenocortical function is low, and then with confidence only if the aldosterone is more than the normal levels quoted.

So far three patients, with diseases in which sodium retention has not previously been reported, have been found with a free steroid in the urine which fulfils the three criteria of aldosterone—namely, reducing property, soda fluorescence, and correct R_F value.

Department of Chemical Pathology,
St. Thomas's Hospital Medical School,
London, S.E.1. IVOR H. MILLS.

GENERALISED MYOKYMIA IN THYROTOXICOSIS

SIR,—In their article in your issue of Sept. 4 Dr. Harman and Dr. Richardson ascribe the lessening of myokymia in a thyrotoxic patient to cure of the thyrotoxicosis.. It is interesting to note that nine to ten months after subtotal thyroidectomy there was still some myokymia present. The sequence of the treatment, employing first an antithyroid drug, methylthiouracil, suggests that other factors than depressed thyroid function may have contributed to the initial improvement in muscle function.

Within four months after starting methylthiouracil (0·6 g. daily) "the myokymia was obviously less." The total duration of drug treatment is not clearly defined, but the thyroidectomy was performed at least fifteen months after the initial administration of the drug.

Attention should be drawn to the fact that thiourea and thiouracil derivatives in certain dosages have pharmacological effects on nerve and muscle activity. Astwood [7] observed in rats a paralysis of motor function from the chronic administration of dithiobiuret, a compound consisting of two thiourea groups. Barfred [8] described an instance of paresis after three months of methylthiouracil therapy (0·8 g. daily). Many forms of neuromuscular disturbance, more appropriately designated as neurotoxic effects, such as paræsthesiæ, vertigo, myoclonic twitching, and loss of taste, have been described with one type or another of every known chemical congener of thiourea or thiouracil. These observations have been summarised by Frawley and Koepf.[9]

The direct effects of these drugs on the neuromuscular system confuse experimental attempts to identify the individual factors concerned in the development of muscle dysfunction in thyroid disease. No less difficult is the interpretation based on clinical observations of this group of drugs.

Department of Endocrinology
and Metabolism,
Albany Medical College,
Albany, New York. THOMAS F. FRAWLEY.

TUBERCULOSIS IN CHILDREN

SIR,—The first reaction to Dr. Bentley's letter last week should be to deprecate discussion of tuberculosis on the basis of age alone. It is now generally recognised that the "childhood type" and "adult type" of tuberculosis are misleading terms. The real basis for clinical or epidemiological action is to classify into primary and secondary types. The primary type may commence at any age, but, of course, most frequently in childhood and adolescence. In a series of 972 chest-clinic cases classified by me into primary and secondary types, there was a gradual increase in the age-incidence of primary disease from infancy to the age period 15–19, with only a slight decrease in the succeeding quinquennium and thereafter a *rapid* decrease. Secondary disease, on the other hand, commences, with few exceptions, in the age period 10–14 and reaches a peak at 20–24, thereafter *gradually* decreasing.[10] Such a striking difference is sufficient to show that, from the point of view of age-incidence alone, primary and secondary tuberculosis are two quite different types. When they are lumped together, as they generally are, confusion at once arises and indications for action become blurred.

Secondly, in spite of Dr. Bentley's attempts to prove that the division between infection and disease "has become untenable," there is a real practical difference between these two concepts. Tuberculous "infection" is a loosely used term to denote diverse and various aspects of the host-parasite contact. "Established infection," however, is the much rarer condition resulting from multiplication of tubercle bacilli in the tissues. The resulting lesion may even then be rudimentary or it may lead to "disease." The term "infection" should be limited to the phenomena of the preclinical stage, and "disease" to the clinical stage, even if that is revealed by nothing more than a positive tuberculin test. The practical point is that we should aim at an exact diagnosis of the type and form of tuberculous "disease" present.

This will include: (1) radiologically invisible benign primary disease with at least a positive tuberculin reaction; or (2) radiologically visible benign primary disease, sometimes complicated by resolving pneumonia, atelectasis, or pleural effusion; or (3) malignant primary disease with its serious sub-forms—lobar caseous pneumonia, bronchopneumonia, or acute miliary tuberculosis. It is only after primary disease, in one or other of these forms, has become quiescent that secondary disease can arise, either by a new exogenous infection (75%) or by autogenous reactivation (25%). Secondary disease includes: (1) the fibrocaseous form starting with the unilateral minimal lesion; and (2) the fibrous form starting with bilateral localised chronic miliary lesions in the apices.[11]

The third point is the "thorny and difficult" problem of notification. Dr. Bentley pleads that all "infected" children should be notified to the chest clinic "in some suitable way" which he admits that he cannot specify. I think he means that all "diseased" children should be so notified—and surely diseased adults also. Notification

6. Luetscher, J. A. jun., Johnson, B. B. *J. clin. Invest.* 1954, **33**, 276.
7. Astwood, C. B., Hughes, A. M., Luben, M., Vanderlaan, W. P., Adams, R. D. *Science*, 1945, **102**, 196.
8. Barfred, A. *Amer. J. med. Sci.* 1947, **214**, 349.
9. Frawley, T. F., Koepf, G. F. *J. clin. Endocrin.* 1950, **10**, 623.
10. Sekulich, M. Tuberculosis: Classification, Pathogenesis and Management. (In the press.)
11. Sekulich, M. Classification of Pulmonary Tuberculosis. London, 1953.

by the practitioner should come *after* an exact diagnosis has been made, either by himself or with the aid of the chest clinic, mass-radiography unit, or other means. A single test, whether tuberculin, X ray, or sputum, will not usually be sufficient. Combined methods of investigation will often be necessary, especially in primary disease. These should enable the type and form of the disease, together with its activity or quiescence to be recorded. Such an exact diagnosis will at once give a lead to the appropriate epidemiological or clinical action. For epidemiological purposes only 9 categories are needed :

I.—*Active forms :* (1) benign primary ; (2) malignant primary ; (3) minimal secondary ; (4) moderately advanced secondary ; (5) advanced secondary ; (6) fibrous secondary ; (7) fibrocavitaria secondary ; (8) non-pulmonary.

II.—*Quiescent forms :* residual lesions of any of the above.

The fourth point is antibiotic treatment. I disagree with Dr. Bentley's "inclination" to support the use of chemotherapy "in certain recent tuberculin converters" with or without primary lesions. This policy would seem to imply massive routine chemotherapy which would almost certainly produce resistant strains on a scale that might be tragic in its consequences. In a series of 34 cases of benign primary disease, including complicated cases, no appreciable effect from chemotherapy was noted either on the pulmonary or lymphatic component. On the other hand it is imperative that malignant primary disease be treated with chemotherapy without delay and preferably in a sanatorium. But this form amounts to less than 1% of primary disease in this country. Benign primary disease is the natural means of immunising vast numbers of the population, for secondary tuberculosis follows quiescent primary disease only in a small minority of cases, probably much less than 1%. Any attempt to sterilise the benign primary disease process prematurely, even if it could be done, might seriously interfere with the natural immunisation of the population. Except for malignant primary and some forms of secondary disease, which should be treated in hospital, the chest clinics can adequately deal with the problem both clinically and epidemiologically. There is no need to segregate in sanatoria, on medical grounds, other than a few cases of benign primary tuberculosis.

The advice of the Ministry of Health to "examine closely our methods and to reinforce them when required" is much needed. Provided that present standards of living in this country can be maintained and increased, our present knowledge of tuberculosis is adequate for the eradication of the disease. But the knowledge which we possess must be applied correctly and that is where present practice is still disturbingly defective.

London, N.W.8. MILOSH SEKULICH.

ŒDEMA AND BELL'S PALSY

SIR,—I wonder whether any of your readers have experience of recurrent Bell's palsy associated with chronic œdema of one side of the face.

A lorry driver, aged 24, with no relevant previous illnesses, developed a left-sided Bell's paralysis in 1950. This came on suddenly and was associated with considerable pain behind the left ear, which lasted for approximately a week. The paralysis was relatively severe but subsided rapidly and was almost completely gone in six weeks, although there was a little residual facial weakness.

Massive œdema of his left face developed two weeks from the onset of the paralysis and has persisted. The œdema is soft and affects particularly the lips and cheeks. It fluctuates widely in severity and he knows of no factor which relieves or aggravates it. In 1952, he had a right-sided Bell's paralysis which completely disappeared in six weeks. No œdema of the right side of the face developed.

Last August he again had a left-sided Bell's paralysis, and this has persisted. The œdema of his left face increased during this last illness and is now beginning to subside. Complete examination and investigation were otherwise negative.

He has been treated with anti-histamines and physiotherapy, and no improvement has been noticed. A search of the literature has not revealed any similar cases.

Law Hospital, Carluke, Lanarkshire. A. MUIR.

INCOMPLETE PITUITARY INSUFFICIENCY

SIR,—If Dr. Wilson and his colleagues, in their article of Oct. 9, were to state the range for their normal controls using the standards of Aub and DuBois, then the figures for the basal metabolic rate, in their interesting cases of incomplete pituitary insufficiency, would be of still greater value.

West London Hospital, Hammersmith, W.6. J. DOUGLAS ROBERTSON.

PANCREATOTROPHIC ACTION OF GROWTH HORMONE

SIR,—In the last few years the attention of many workers has been directed to the study of the relationship between growth hormone (G.H.) and the endocrine pancreas. Recent work deals with the amount of islet tissue and the ratio of islet tissue to acinar tissue in normal and in hypophysectomised rats [1] and in normal, in hypophysectomised, and in G.H.-treated rats on different diets [2] ; the cytology of the islet tissue [3] ; and the ratio of alpha to beta cells.[4] It has been shown that colchicine-induced mitosis of the islet cells is greater in G.H.-treated rats,[5] and that the endocrine pancreas of adult dwarf mice, which resembles closely that of newborn ordinary mice, changes to a more mature type under treatment with G.H.[6]

In a study of maturation of the pancreas I have examined serial sections of the whole pancreas in newborn and in adult albino rats before and after hypophysectomy and treatment with G.H. My principal findings are as follows :

(1) In adult rats hypophysectomy leads to atrophy of the acinar tissue, thus reducing the size of the pancreas. The islet tissue (total volume, total number, and average diameter of islets) is much less than in normal rats of similar age but is comparable in amount to that of normal younger rats with a pancreas of the same size.

(2) The treatment of hypophysectomised rats with G.H. cause hypertrophy of the acinar tissue but does not affect the islet tissue. (The controls were injected with physiological saline solution.)

(3) In all the specimens of pancreas from adult rats the ratio of alpha cells to beta cells in the islet tissue was normal—i.e., about 25 alpha cells to 75 beta cells.

(4) In young rats aged 2–5 weeks the pancreas is not yet mature ; there are about 35 alpha cells to 65 beta cells ; and the amount of islet tissue, in relation to acinar tissue and body-weight, is less than in adult rats.

(5) The ratio of 25 alpha cells to 75 beta cells in the adult rat is reached in about 2 months from birth and is independent of body-weight and intake of food.

(6) Hypophysectomy produces in young rats the same changes as in adult rats as regards the amount of acinar tissue

1. Bryans, F. E., Kinash, B., Ashworth, M. A., Haist, R. E. *Diabetes*, 1952, **1**, 358.
2. Haist, R. E., Kinash, B. *Fed. Proc.* 1951, **10**, 58. Kinash, B. MacDougall, I., Evans, M. A., Bryans, F. E., Haist, R. E. *Diabetes*, 1953, **2**, 112.
3. Abrams, G. D., Baker, B. L., Ingle, D. J., Li, C. H. *Endocrinology*, 1953, **53**, 252. Kracht, J. *Naturwissenschaften*, 1953, **40**, 607.
4. Ferner, H., Tonutti, E. *Z. Zellforsch.* 1953, **38**, 267. Thiemer, K. *Endokrinologie*, 1953, **30**, 176.
5. Cavallero, C., Mosca, L. *J. Path. Bact.* 1953, **66**, 147.
6. Cavallero, C., Dova, E. *Acta path. microbiol. scand.* 1954, **34**, 201.

and the ratio of islet tissue to acinar tissue, but the ratio of 35 alpha cells to 65 beta cells is maintained even into adult age.

(7) In hypophysectomised young rats treated for an adequate time with an adequate dosage of purified G.H. administered soon after the hypophysectomy the changes produced in body-weight, acinar tissue, and the ratio of islet tissue to acinar tissue are the same as those produced in adult rats, but the ratio of alpha cells to beta cells remains unchanged.

These findings suggest that some pituitary factor other than growth hormone is responsible for the development from the juvenile to the adult type of the ratio of alpha to beta cells.

I wish to thank Prof. H. R. Dean for his interest in my research; Prof. F. G. Young for a generous supply of growth hormone; Dr. K. C. Dixon for invaluable advice; and Mr. M. P. Stack-Dunne for undertaking numerous hypophysectomies.

Department of Pathology,
University of Cambridge. LEONARDO MOSCA.

THE ROYAL MARSDEN HOSPITAL

SIR,—As you reported last week, the name of the Royal Cancer Hospital has been changed. The hospital was founded in 1851 by William Marsden, M.D., as The Cancer Hospital (Free). The name has since been varied by adding the prefix Royal when this was commanded, and dropping the word Free on the inception of the National Health Service.

Now, in the interest of patients sent to the hospital, and their relatives, it has been decided to suppress the word Cancer in the name. The Queen has been graciously pleased to approve the continued use of the prefix Royal and the adoption of the name The Royal Marsden Hospital. The work of the hospital continues as before to be the treatment of cancer and allied diseases.

There will be no change in the name of the associated postgraduate institute which will continue to be known as the Institute of Cancer Research: Royal Cancer Hospital.

Royal Marsden Hospital,
London, S.W.3. J. D. BANKS
House Governor.

THE HUMALACTOR

SIR,—After the recent discussion on the humalactor, you will perhaps allow comment from one who is not engaged in the maternity and child-welfare field and who possibly, therefore, approaches the subject with an open mind.

I have recently had daily experience of the apparatus for six months during which the instrument was used to provide complete breast-milk feeding for a child unable to suck because of a hare-lip and cleft palate. The humalactor is an ingeniously devised *instrument* for applying negative pressure to the nipple continuously and evenly, the pressure being regulated by the patient so that the process is virtually painless (which is more than can be said of either the breast pump or manual expression, save in the hands of the most expert).

In the special circumstances of continued feeding with breast-milk over a period of six months there can be little doubt that the instrument is to be preferred to manual expression—which is both slower and more trying to the mother, as is the use of the breast-pump. If it be said that it is useless to try to feed a baby with these defects with breast-milk, I can but say that the surgeon who operated for repair of the defects expressed his surprise at the excellent condition of the child compared with that of the majority of the infants operated on at the age of 3 months.

No doubt these instruments may give some trouble when the users will not take the trouble to familiarise themselves with the working of the machine; but this is true of any complex apparatus (even the automobile) and cannot validly be advanced as an argument against the use of any apparatus.

In our experience the instrument worked flawlessly for six months of continual use—four or five times daily. One could not speak more highly of the mechanical efficiency of any apparatus. There is little doubt in my own mind that such apparatus has its place in a maternity unit and that the comfort of the mother and the cause of breast-feeding can both be advanced by the reasoned use of the humalactor.

Rainow,
near Macclesfield, Cheshire. A. HOLMES-SMITH.

NON-GONOCOCCAL URETHRITIS

SIR,—In your annotation of Oct. 2 you say that urethritis originating from *Trichomonas vaginalis* infections is recognisable clinically. In my own experience the only specific clinical manifestation is a characteristic urine which is often associated with heavy urethral infections with *T. vaginalis*. In light and transient infections this is not present, and diagnosis in these cases depends on the usual laboratory procedures. Further information on this point would, I am certain, be of interest to many.

F. LANCELEY
Liverpool Royal Infirmary. Assistant Venereologist.

*** The discharge in trichomonas vaginitis is often thin, milky, and frothy. This type of infection can, of course, be identified with certainty only by seeing protozoa under the microscope; but early recognition is important clinically because this infection carries no risk of complications such as arthritis and conjunctivitis and is not affected by the usual antibiotics. On the other hand, classification into urethritis with inclusion bodies and urethritis with pleuropneumonia-like organisms is no great help to the clinician, because there is apparently no difference in the course of the infections or in their treatment.—ED. L.

IDIOPATHIC HYPERCALCÆMIA OF INFANTS: LOW-CALCIUM TREATMENT

SIR,—In your issue of June 19, Dr. Ferguson and I described methods of producing low-calcium milk.[1] The first method used a resin column, which was conditioned by treatment with a solution containing sodium, potassium, and magnesium at about forty times the concentrations found in cow's milk. Unfortunately the concentration of magnesium sulphate was given as 2·4 *M*, whereas the correct value should be 0·24 *M*. (As stated in our paper, milk contains 10 m.eq. of magnesium per litre—i.e., a concentration of 0·01 *N* or 0·005 *M*.)

In our most recent work we have used magnesium chloride (also 0·24 *M*) in preference to the sulphate, in order to prevent precipitation of calcium sulphate.

Bristol. G. K. MCGOWAN.

MUSCLE SPASM AFTER HYDROCELE OPERATION

SIR,—A bilateral hydrocele was treated by excision of the sac on the right side and eversion on the left, through separate scrotal incisions. Nothing unusual was noted until the patient was asked to get out of bed on the fourth day, when he complained of painful cramp in the left half of the hypogastrium and along the left spermatic cord. The cramp prevented him from fully extending his trunk and left thigh. It was relieved the moment he lay down.

The wounds were found to be clean, but there was some œdema and hyperæsthesia of the scrotum, more on the left side. The left testis and epididymis were enlarged to about thrice the normal size and were acutely tender. The right side was similarly affected in a minor way. Both spermatic cords were normal and could be rolled on the pubic crests without

1. Ferguson, A. W., McGowan, G. K. *Lancet*, 1954, i, 1272.

undue discomfort to the patient. The abdomen was soft and the thighs could be actively hyperextended.

This case presents two interesting features:

(1) Absence of spontaneous pain due to epididymo-orchitis during recumbency.

(2) Painful muscular spasm induced by the drag exerted by the inflamed testis on the spermatic cord on standing. The spasm was probably most severe in the left conjoined tendon and cremaster. The nerves involved are associated with the 10th thoracic to the 2nd lumbar segments of the cord.

The cramps were no longer provoked on standing when the testicular inflammation became less acute.

Faculty of Medicine,
University of Malaya,
Singapore.

A. MOHIUDDIN.

ŒSTROGENS AND MENOPAUSAL UTERINE BLEEDING

SIR,—Synthetic œstrogen drugs are widely and effectively used for a variety of menopausal complaints; but if given too long, or in too large doses, they cause endometrial hyperplasia and abnormal uterine bleeding.[1–4] The bleeding may occur either during therapy, the thickened endometrium being shed by reason of its sheer weight, or at any time up to six weeks from the cessation of therapy, owing to the endometrium crumbling. Hospital investigation is advisable in every case under œstrogen therapy in which abnormal bleeding occurs.[5] Moreover, endometrial hyperplasia and carcinoma are so closely related, as pointed out first by Novak and Yui,[6] that synthetic œstrogens which are known to cause the one must be suspected of causing the other.

TABLE I—PILOT INQUIRY, 1952

Endometrial condition	History of œstrogen therapy	No history of œstrogen therapy	Total
Non-secretory cystic hyperplasia ..	7	27	34
Other endometrial conditions (secretory cystic hyperplasia, endometrial atrophy, endometrial carcinoma) ..	0	37	37
Total	7	64	71

At the Jessop Hospital for Women, Sheffield, an inquiry was carried out to determine whether the number of cases of uterine bleeding due to synthetic œstrogens has been increasing with the greater employment of these drugs and whether there has been any concurrent rise in the incidence of endometrial carcinoma.

TABLE II—THE FIGURES FOR 1948–52

Year	Non-secretory cystic hyperplasia	Receiving œstrogen therapy	Endometrial carcinoma
1948	21	0	27
1949	15	0	23
1950	28	2	16
1951	40	8	31
1952	34	7	16
Total ..	138	17	113

A pilot inquiry was first made, limited to patients over 50 investigated during 1952, for menopausal menorrhagia or postmenopausal bleeding. Of 71 such cases 7 had been given œstrogen; in each the endometrial condition was non-secretory cystic hyperplasia (table I).

Further study was therefore restricted to those women over 50 whose uterine endometrium showed non-secretory cystic hyperplasia or adenocarcinoma. All case-records over a five-year period (1948–52) were scrutinised. The results are given in table II. Thus, the number of cases of menopausal menorrhagia and postmenopausal bleeding requiring hospital investigation, and the number of these given synthetic œstrogens, appears to be increasing; the incidence of endometrial carcinoma, on the other hand, has not altered.

The œstrogen therapy in these cases was most commonly given for hot flushes or other nervous symptoms, and occasionally in an effort to control irregular bleeding. The œstrogens were usually given by mouth. Sometimes, stilbœstrol pessaries were employed for senile vaginitis, or œstrogen-containing creams were liberally applied to the vulva in cases of pruritus. Treatment was often prolonged, occasionally for as long as two years at a time.

This inquiry, therefore, has indicated no association between prolonged œstrogen therapy and carcinoma. It suggests, however, that despite the warnings of previous authors on this subject, overdosage with synthetic œstrogens continues to cause much distress to menopausal and postmenopausal women, and an increasing amount of unnecessary hospital investigation for abnormal uterine bleeding.

My thanks are due to Dr. C. G. Paine for allowing me access to laboratory records, and to Prof. C. Scott Russell for advice and encouragement.

Sheffield. J. G. NAPIER.

LIABILITY FOR ACTS OF DEPUTY

SIR,—I am grateful to Dr. Noy Scott for the technical correction concerning my use of the phrases "group of doctors" and "as a body" in my letter of Sept. 25. Neither Dr. Noy Scott nor anyone else, however, has attempted to answer the question posed: How does one take greater care in one's deputising arrangements in a partnership practice than by asking one's partner to see a case?

The absence of a reply suggests that the medical members of the medical services committee concerned had not taken a firm enough stand collectively—i.e., as a body of informed opinion in the committee—in pointing out to the lay members the difficulty inherent in the position they were adopting. In this event I submit that it was a group of doctors—in this instance 3 out of a total of 7 members, medical and lay—who were responsible directly or indirectly for this controversial recommendation.

Penketh, Lancs. T. S. EIMERL.

USE OF THE SAC IN REPAIR OF INGUINAL HERNIA

SIR,—In Bassini's operation for the repair of inguinal hernia the canal is opened and the sac cut away before or after isolating the spermatic cord. Repair of the posterior wall of the canal is often hampered by the difficulty of closing completely the inner end of the gap between the internal oblique and transversalis muscles and the inguinal ligament. The use of the sac for closing this defect has apparently been overlooked. I have used the method for years, with good results.

The inguinal canal is opened, and the cord freed and raised. If it looks as if the sac may be needed its neck alone is isolated and ligatured, and the severed stump is allowed to retract. Repair is then begun in the usual way, medial to the internal ring. If repair can be effected easily, the sac is stripped from the cord and discarded. If a gap persists medially which cannot be closed, its margins and the sac lying on the back of the cord are isolated, and the free edges of the sac are sutured to the margins of the gap. Should the sac prove too large, as commonly it is, its fundus is freed further, grasped on the inner aspect with forceps passed into the open neck,

1. Novak, E. R. *J. Amer. med. Ass.* 1944, **125**, 98.
2. Cheek, D. B., Davis, J. E. *Amer. J. Obstet. Gynec.* 1946, **52**, 756.
3. Feeney, J. K. *J. med. Ass. Eire*, 1947, **20**, 260.
4. Sutherland, A. M., McBride, J. M. *J. Obstet. Gynæc., Brit. Emp.* 1954, **61**, 238.
5. Kanter, A. E., Klawans, A. H. *Surg. Clin. N. Amer.* 1950, **30**, 287.
6. Novak, E. R., Yui, E. *Amer. J. Obstet. Gynec.* 1936 **32**, 674.

and invaginated the required distance. A pad of four layers of peritoneum, in situ, and with a blood-supply from the cord, is thus available for suturing into the margins of the defect. The remainder of the operation is completed in the usual way.

By this method the need to introduce foreign materials or to journey down the thigh in search of fascia is avoided.

Newcastle upon Tyne. F. C. PYBUS.

CHLORPROMAZINE IN MENTAL DEFICIENCY

SIR,—The shortage of nurses at most mental-deficiency hospitals makes the care of defectives who are aggressive, destructive, or subject to self-mutilation particularly difficult.

For the past nine months at this mental-deficiency institution of 700 beds, and at several smaller similar institutions, improvement in conduct disorders has followed the oral administration of chlorpromazine hydrochloride ('Largactil') in daily doses of 75–400 mg.

Of 32 cases thus treated, 5 improved dramatically, 19 improved distinctly, and 6 failed to respond. Low-grade defectives improved more commonly than high-grade. In those whose condition was improved, destructiveness and aggressive tendencies were noticeably diminished and hyperkinetic activity ceased; and the improvement extended to their physical state with increased appetite and weight and improved physical appearance.

No serious side-effects were encountered, but 3 of the patients had slight pyrexia (99°F) for a few days during the first ten days of treatment; this subsided without the drug being withdrawn. 9 of the patients became especially sensitive to changes in environmental temperature.

The effect has been to greatly improve the social conduct of such patients.

Hensol Castle, near Pontyclun, Glam. T. S. DAVIES.

WHAT IS LABILE-POOL IRON?

SIR,—It is commonly held that before exogenous iron is built into hæmoglobin, it undergoes dilution in a certain fraction of body iron, the quantity and turnover rate of which have already been estimated. This idea is based on the interpretation of data collected in experiments with Fe^{59}.

The fraction in question has been severally defined as the "labile-pool iron,"[1] "a very small labile iron reserve,"[2] or the "topsoil of iron stores."[3] Moreover, the notion has been extended to endogenous iron derived from physiological hæmolysis.

The existence of a labile-pool iron has been admitted for the following reasons.[1] Taking into account the average life of red cells and the amount of hæmoglobin iron in normal man, then the quantity of iron released daily from destroyed erythrocytes and the quantity used each day for hæmoglobin synthesis is about 24 mg. If 5 mg. of intravenous Fe^{59} is introduced, then, on the first day, 83% of the radioactive iron given ought to be embodied in the circulating Hb ($24 \times 5 : 24 = 100 : 83$); but, instead of that, it is only possible to find a mere 10% of the Fe^{59}.

Finch et al.[2] found that 50% of the Fe^{59} utilised for hæmoglobin synthesis appears in circulating red cells in 2·2 days. Hence they state that before radioactive iron is built into hæmoglobin it is first diluted in a fraction of the iron stores, 50% of which turns over every 2·2 days. Considering that 24 mg. of iron is required daily for normal erythropoiesis, they come to the conclusion that the fraction in question amounts to about 100 mg. ($24 \times 2 \times 2{\cdot}2$).

We believe that an exact quantitative estimate of the fraction of body iron, in which the labelled iron is diluted, may be made only by taking into account the *utilisation rate of radioactive iron by the erythropoietic tissue*, and not by basing the estimate on the appearance rate of radioactive iron in circulating red cells. As a matter of fact, the argument set forth by Greenberg and Wintrobe[1] and by Finch et al.[2] would be valid only if both utilisation and appearance took place at exactly the same time.

On the other hand, iron is taken up by all the cellular elements that make up the erythropoietic tissue, from the basophil erythroblasts, to the reticulocytes, each reaching complete maturation at a different time. The labelled Hb therefore enters the blood-stream at different intervals according to the maturation stage at which the utilisation of radioactive iron has occurred. These intervals extend over a long period—about 3 days—for 3 days is the average maturation time of the normoblast, reckoning from the moment it may take up iron till it enters the blood-stream as a reticulocyte.

The quantity of iron utilised every instant by the erythropoietic tissue represents the total amount of the fractions utilised in that same instant by the single erythroblasts. These fractions vary according to the maturation stage the erythroblasts happen to have reached, and more exactly, the closer the erythroblast is to its full maturation stage the smaller these fractions are. Similarly, the fraction of iron embodied in an erythroblast decreases as a function of time while maturation is progressing.

As it stands, the appearance rate of radioactive iron in circulating red cells is a function of the utilisation rate of radioactive iron by erythropoietic tissue, taking into account that the fractions of iron utilised for erythropoiesis at any moment are: (1) embodied in each single erythroblast in varying quantities, according to the maturation stage it happens to be in; and (2) liberated into the circulation successively during 3 days.

We have calculated the fraction of radioactive iron utilised daily by the erythropoietic tissue, starting from the data we have collected, concerning the fractions of radioactive iron entering daily into the circulating hæmoglobin. The estimation has been made by resorting to successive approximation, postulating that:

(1) The fraction present in the circulating red-cell mass when the first day is over is the amount utilised by cellular elements that have completed their maturation within 24 hours.

(2) The fraction utilised by the erythropoietic tissue on the first day is at least the same as that appearing in circulating red cells on the third day.

The data collected are confirmed by the results of the mathematical analysis.

We have thus found that 50% of radioactive-iron utilisation takes place in 1·5 days—namely, within half the average time, as reckoned from the moment a normoblast starts taking up iron till the reticulocyte is liberated into circulation. Hence, the tracer is mixed in 3 days with the iron needed for 3 days' erythropoiesis ($24 \text{ mg.} \times 3 = 72$).

A proof is therefore furnished that iron destined for hæmoglobin synthesis is immediately involved in erythropoiesis. The so-called labile-pool iron is merely that fraction of hæmoglobin iron embodied in the erythropoietic tissue. There is, therefore, no need to accept the existence of a fraction of stored iron in which the iron would be diluted before being used in hæmoglobin synthesis.

Department of Medical Pathology, University of Rome. UGO SALERA
GIACOMO TAMBURINO.

1. Greenberg, G. R., Wintrobe, M. M. *J. biol. Chem.* 1946, **165**, 397.
2. Finch, C. A., Gibson, J. G., Peacock, W. C., Fluharty, R. G. *Blood*, 1949, **4**, 905.
3. Dubach, R., Moore, C. V., Minnich, V. *J. Lab. clin. Med.* 1946, **31**, 1201.

Obituary

MAURICE PERCY CUE HOLT
K.C.B., K.C.M.G., D.S.O., M.R.C.S.

Major-General Sir Maurice Holt, who died on Sept. 6 at Farnborough, at the age of 92, became an Army doctor in 1887, and when he retired in 1922 he had completed thirty-four years of distinguished service.

Entering King's College Hospital from King's College School he qualified in 1886. Within the year he had begun his Army career, and by 1895 he was in medical charge of the expedition to Sambana's and North Zululand. For this piece of work he received the thanks of the Colonial Office. In 1899 he was promoted major, and for the next three years he saw active service in South Africa. He was present at the actions at Elandslaagte, Rietfontein, and Lombards Kop, and at the defence of Ladysmith. He was mentioned in despatches and in 1902 appointed D.S.O. He was already a surgeon specialist and he contributed to the *Report on Surgical Cases in the South African War*, the section on the chest and neck. After the war he lectured on operative surgery at the Royal Army College, Millbank, and to this period belong his papers on fractures and dislocations of the carpal bones, on hernia, and on the treatment of persistent urinary fistula. Later he served in India and in 1911 he became surgeon to the Viceroy.

Soon after the outbreak of war in 1914, Holt was appointed A.D.M.S. of a division, and in 1915 director of medical services for the Salonika Field Forces. For his services he was made C.B. in 1915 and K.C.M.G. in 1917, and promoted K.C.B. in 1919. His foreign decorations included appointments in the Legion of Honour, the Order of the Redeemer, and the Order of the Star of Rumania. From 1919 to 1922 he was honorary surgeon to the King. In 1922 he retired from the Service, but from 1928 to 1932 he was colonel commandant of the R.A.M.C.

A. G. W., who knew Holt first in India and later in France, writes:

In 1911 I was sent to Kasauli to do surgery under him. He was then commanding the British Military Hospital, and soon after, I took over as surgical specialist when he became consulting surgeon to Northern India. "Mickey" was a great man in all but stature—a very able surgeon, a first-class administrator, a strict but fair commanding officer, and, when one got to know him well, a friend such as are rarely met. At this time he became widely known as an obstetrician, and ladies came from distant stations to have their babies under his care, my own wife among them.

He would not tolerate slackers of any description, but a trier was assured of every possible help and encouragement. I owed much to him, and I never forgot the many lessons and skilled demonstrations he gave me in surgical technique. He was a follower of Arbuthnot Lane in bone surgery, and his results were excellent.

Holt was a great horseman and a lover of horses. He had many other hobbies of which perhaps his greatest was cabinet-making and carpentry, at which he was an expert. He was a keen gardener and, perhaps unknown to most people, a very fine organist. My wife and I have kept in touch with him ever since his retirement, and if we were in England, we always tried to visit him on his birthday. We did so this year when he was 92, and we found him gardening, as indeed he was the day before he died.

He was a man whose aim was always to do good when he could, who hated publicity, and who never spoke of his many attainments. He outlived his own generation, but those of us somewhat younger who knew him mourn a very dear friend.

From early manhood he had been keen on sailing, and in retirement he got much pleasure from the yacht which he kept on the Hamble. With the manual versatility of the surgeon and sailor he also possessed and retained a versatility and vigour of mind which continued to delight his friends.

In 1887 he married Sarah Annie, daughter of Thomas Busteed of Madras, and she survives him with a son and daughter of the marriage.

Notes and News

DISTRIBUTION OF ANTIBIOTICS

THE Ministry of Health has arranged for tetracycline to be made available to hospitals in the National Health Service from Oct. 15 in forms suitable for oral administration and injection, including forms suitable for oral administration to young children. At the same time tetracycline will be made available to general practitioners through the regional distribution centres from which aureomycin and terramycin (oxytetracycline) are now obtained and for the same conditions as are specified for these two antibiotics. The Ministry has been advised by the Medical Research Council that tetracycline is suitable for treatment of the same conditions and its toxicity is also similar, so that the same precautions should be observed in its use.

The Ministry has also arranged with the manufacturers concerned for aureomycin and terramycin to be available on prescription from Nov. 1. The Ministry points out that the drugs should in general be reserved for cases of serious infection with micro-organisms insensitive to sulphonamide and penicillin. In severe staphylococcal infections resistant to penicillin, but sensitive to aureomycin and terramycin, one of the latter should be selected as the drug of choice. But their general use, either systemic or local, in minor staphylococcal infections will foster the emergence and spread of resistant strains throughout the population. The drugs are also indicated in the treatment of brucellosis, bacillary dysentery resistant to sulphonamide, and infection with viruses of the psittacosis group, such as psittacosis and lymphogranuloma venereum. Their effect on pertussis is less certain and is confined to the first week of disease and perhaps to immediate prophylaxis in infants exposed to infection. In the treatment of clinical pneumonia clinical trials have shown that patients treated with aureomycin fare no better than those on penicillin and are more liable to suffer from side-effects. Prolonged treatment of chronic chest infections is unlikely to be of value. In pyelitis and cystitis not responding to the usual treatment, the drugs are of value if the organisms are sensitive. Although the typhoid bacillus is sensitive, enteric fever is not controlled by aureomycin or terramycin. The effect of aureomycin in infantile gastro-enteritis is doubtful. Since neither drug given orally can be relied upon to reach the cerebrospinal fluid in decisive concentrations, they are less suitable than sulphonamides in meningococcal meningitis or chloramphenicol in influenzal meningitis; the combination of penicillin with aureomycin or terramycin in the treatment of pneumococcal meningitis is absolutely contra-indicated. Apart from the control of secondary infection, neither drug influences virus diseases, except those of the psittacosis group.

Sir PATRICK MANSON

FOR his Manson lecture, given on Oct. 5 at the London School of Hygiene and Tropical Medicine, Sir Philip Manson-Bahr chose the title: "Patrick Manson: the Father of Tropical Medicine and Founder of the School of Tropical Medicine." In an informal study of Manson's life and work, the lecturer recalled his unsurpassed contributions to the knowledge of filariasis and malaria, as well as his influence on the men who worked under him. In his later years he was regarded by his juniors almost as a god; but Manson himself preferred to be known simply as the best snipe-shot in China.

After graduating at Aberdeen in 1864, Manson spent five years in Formosa, "living the life of a tea-planter." During this time he acquired the surgical technique which he later perfected as physician to the mission hospital at Amoy. At Amoy he began work on filariasis, and by 1874 he was able to announce proudly that he had "removed over a ton of scrotal elephantiasis." In 1875 he returned to England, and in the reading-room of the British Museum met Timothy Lewis, "the godfather of tropical medicine," whose discovery of *Filaria sanguinis hominis* fired him with fresh enthusiasm. Back in China, with a wife and a microscope—"both the best procurable"—he demonstrated, by painstaking investigations on his Chinese gardener, that the embryo filariæ passed through a stage of their cycle in the mosquito, and appeared in the patients' blood only after sunset. His second great achievement—the conception of the "mosquito-malaria hypothesis"—was at first ridiculed almost everywhere, but the India Office was sufficiently impressed to second Ronald Ross to investigate malaria in India. Manson gave great assistance

to Ross—more than 120 letters passed between them—and in 1897 Ross wrote to him triumphantly of his discovery of the malarial parasites in the stomach of the anopheline mosquito: this historic document is now preserved in the present School of Tropical Medicine.

The school was established originally on an unimposing site near the Albert Dock, close to the Seamen's Hospital. "An important feature was its proximity to the Connaught Arms, where there was inferior beer and very bad company." Before long Manson had gathered round him a brilliant and devoted staff, and he lived to see the school achieve an international fame.

Sir Philip's lecture was illustrated by a large number of photographs, many not previously shown in public. Dr. Andrew Topping, dean of the London School of Hygiene and Tropical Medicine, presided.

OCCUPATIONAL THERAPY EQUIPMENT

To prescribe regular exercise for a weak muscle, or movement for a joint, is easy; but often much ingenuity is needed to fulfil the prescription to the satisfaction of both doctor and patient. Those who have to solve anatomical and mechanical problems of this kind will find it useful to study an illustrated account, by Mrs. Jones,[1] of the equipment used at Farnham Park Recuperative Home. This includes a bicycle saw and filing machine, for improving muscular power after hip arthroplasty, and an ankle rotator saw for promoting recovery from leg or foot injuries. Foot-powered lathes have been adapted to encourage knee-movements of up to 170°–80° in range, and are used at all stages of progressive weight-bearing. Foot-driven looms provide gentle leg exercises for patients with associated disease of the heart; these are also useful in hastening the return of coördination after cerebral or cerebellar injuries. The equipment was constructed partly by the patients themselves in the course of treatment, and old-fashioned machines sometimes proved particularly suitable for adapting, since older machines are more often foot-powered than newer models.

All the occupational therapy at the home is strictly supervised to make certain that patients get as much benefit as possible from their treatment. More than 1200 patients with injury or paresis of the lower limbs were treated between 1947 and 1953.

MUSCLES IN ACTION

ANATOMY, some fancy, is a dead-end subject; whereas anatomists claim that their work is barely begun. Ever since they turned their eyes from the cadaver to the living body they have been finding that explanations of structure and action, which we have long taken for granted, need some drastic revision. Muscular activity, for instance, has been described in terms that are far too simple. As students, we learned origins and insertions, and believed that when a muscle shortened between these two points we could state precisely the effect on the intervening joint. Far from it: what a muscle does to a joint depends not only on what other muscles are doing at the time but also on which of its own fibres are called into play.

Prof. W. E. Le Gros Clark, F.R.S., discussed some of the implications of this at a symposium arranged by the Ergonomics Research Society in 1951, the report[2] of which, edited by Mr. W. F. Floyd, PH.D., and the Rev. A. T. Welford, has now appeared. The functional units of which each muscle is composed—called "motor units"—may come into action, he points out, at different phases of each movement, and may show quite different patterns of activity when the muscle is used for different purposes. The innervation of these motor units proves to be exceedingly complex, and their activities can be studied by electromyographic techniques. If a muscle is contracted voluntarily, and the same movement is made over and over again, the same motor units come into action in the same sequence; but if the movement is slightly varied, the sequence of activity of the motor units also varies. Again, if the original movement is combined with some other movement, involving the same or an associated group of muscles, the sequence of activity of the motor units may form yet another pattern. Thus we think of the biceps as flexing the elbow-joint; but if flexion of the elbow is combined with pronation of the forearm, the activity of the motor units in the biceps diminishes, finally disappearing altogether; and in fact in this combined movement the elbow is flexed not by the biceps but by the flexor carpi radialis. Le Gros Clark quotes Seyffarth's summary of these and similar findings: when two movements are simultaneously performed there is not a simple summation of the synergies of the two movements, but the production of a new synergy.

Electromyographic techniques, in revealing precisely which muscles or muscle groups take part in elementary movements, have proved that muscles may be quite inactive in movements and postures where they have always been supposed to take an important part. Thus muscles are not as responsible as we have always supposed for maintaining natural postures: the thigh muscles, when we stand upright, do not brace the hip and knee-joint by their tonic contraction—on the contrary, they are electrically silent. The anterior tibial group of muscles do not, after all, hold up the arch of the foot: they leave it to the ligaments. This means that the ligaments will have to be studied afresh. Then the anatomy of muscles is not the straightforward strap arrangement that it once seemed. The complex pattern of innervation is matched by a complex arrangement of fasciculi of varied length disposed at many different angles. How these differences affect the mechanics of the muscle is still to be studied.

The details of lymphatic drainage, too, are still unknown. Since the metabolites formed by muscular action are presumably removed by the lymph, and the rate at which they are removed presumably helps to determine the rate at which fatigue sets in, the distribution of the ultimate lymphatic capillaries is of much practical interest. All these studies, indeed, relate to practical matters; for the design of modern machinery, whether in industry or for transport, turns much on the position in which muscles can act not only powerfully but economically, so that fatigue is prevented or postponed.

Again, these studies have medical applications. Thus we all know that a muscle which is regularly exercised develops in size; and this hypertrophy is probably associated with increased efficiency of the blood vascular supply, and perhaps with proliferation of new capillaries, so that capillary density is increased. But it has been observed that such "training" of one arm is associated with some increase of size in the muscles of the other arm, which has not been used. This may be due, Le Gros Clark suggests, either to a peripheral reflex mechanism or to "some central adjustment in the activities of the nervous system." Either way it might have considerable practical importance, he says, in the treatment of muscles which are recovering from paralysis caused by a nerve injury.

1. Jones, M. S. *Brit. J. phys. Med.* 1954, 17, 169.
2. Symposium on Human Factors in Equipment Design. London: H. K. Lewis. 1954. Pp. 132. 21s.

University of Cambridge

Dr. C. C. D. Shute has been appointed a university demonstrator in the department of anatomy.

Welsh National School of Medicine

Dr. Paul Fourman has been appointed senior lecturer in medicine, Mr. H. J. Fisher, senior lecturer in obstetrics and gynæcology, and Dr. W. R. L. James, senior lecturer in forensic medicine.

International Federation of Medical Student Associations

The third general assembly of this federation met in Rome on Oct. 1–5, with Mr. Erwin Odenbach (Western Germany), the president, in the chair. Great Britain, represented by the British Medical Students' Association, was elected chairman-nation for 1954–55. A resolution was passed refusing further contact with the International Union of Students, while welcoming contact with any medical students who desired to coöperate on the basis of the I.F.M.S.A. constitution, which expressly excludes political issues from the work of the federation.

Standard of Students

In his annual report at the opening of the new session (*Times*, Oct. 9), Dr. E. C. Warner, dean of Charing Cross Hospital Medical School, said that first-year medical students were nowadays not as good as had been hoped, despite careful selection. They did not seem to have the same sense of vocation as students of previous years. In second-year students there were signs of the same lack of determination and keenness. Students who came from the Forces at the end of the war set a high standard which was an inspiration to themselves and to their teachers. What a pity it was, Dr. Warner observed, that this standard had not been maintained.

Royal Medical Foundation of Epsom College

Mr. R. W. Raven has succeeded the late Dr. Harold Spitta as chairman of Epsom College Council. Brigadier H. L. Glyn Hughes has succeeded Sir Ernest Goodhart as vice-chairman.

War Memorial

On Tuesday, Nov. 2, at 3 P.M. the Archbishop of Canterbury will dedicate at B.M.A. House, London, the Memorial to doctors of the British Commonwealth who fell in the war.

Society of Anæsthetists of South Wales

This society is to hold its annual dinner meeting at the Park Hotel, Cardiff, at 7.30 P.M. on Thursday, Oct. 21. The guest speaker will be Prof. W. W. Mushin, whose subject will be An Anæsthetist in Brazil.

Library Association

At a meeting of the association's medical section, to be held at Chaucer House, Malet Place, London, W.C.1, at 7 P.M. on Friday, Oct. 29, Dr. A. H. T. Robb-Smith will speak on the History of Nosology.

Yorkshire Association of Graduates of Glasgow University

The annual dinner of this association will be held in the Victoria Hotel, Bradford, on Friday, Oct. 22. The secretary of the association is Mr. James Wishart, 33, Manor Row, Bradford.

Hypnotherapy Group

A clinical meeting of this group will be held at the Eastman Dental Hospital, Gray's Inn Road, W.C.1, on Wednesday, Oct. 20 at 8 P.M. There will be a number of short papers on hypnosis in medicine; the speakers will be Dr. William Moodie, Dr. Stafford Clark, Dr. George Newbold, Dr. Gordon Ambrose, Dr. Kathryn Cohen, and Mr. Eric Wookey.

CORRIGENDA: *World Congress of Cardiology.*—We regret that in our report of Oct. 2 (p. 701) we erroneously stated that Dr. W. G. A. Swan was a speaker at Washington. The Dr. Swan who described blood-flow patterns through atrial septal defects was Dr. Henry Swan, of Denver, Colorado.

King's College Hospital Medical School.—This school's annual dinner was attended by 279 past and present students and guests—not 160 as we stated last week (p. 765).

Births, Marriages, and Deaths

BIRTHS

JAMES.—On Oct. 2, to Elisabeth C. W. James, M.B. (née Withers), wife of Derrick W. James, M.B.—a son.

DEATHS

REES.—On Oct. 4, after a short illness, Mary Isabel (Dr. Hemingway Rees), beloved wife of Dr. J. R. Rees, 116, Bickenhall Mansions, W.1, and mother of Elisabeth Medley.

Appointments

BARNES, ROY, M.R.C.S., C.P.H.: senior asst. M.O. and school M.O., Yorkshire, Div. 25 (Wombwell).

BEVERIDGE, ELSPETH V., L.R.C.P.E., D.P.H.: asst. M.O.H., Perth and Kinross.

DAVIES, C. E., M.A., D.M. Oxfd, M.R.C.P., part-time consultant physician, Royal Hospital Unit, Sheffield.

FOGARTY, OONAGH M., M.B.N.U.I., D.C.H.: school M.O., Nottingham.

FYFE, GEORGE, M.B. St. And. D.P.H.: divisional M.O., Lancashire, health division no. 13 (Heywood).

GARRATT, F. N., M.B. Birm.: asst. M.O.H., Walsall.

IRVINE, D. J. McI., M.B. Edin., M.R.C.O.G.: obstetrician and gynæcologist, Royal Infirmary, Edinburgh.

JOEL, MARY B. F., M.B. Edin.: asst. M.O., maternity and child welfare, Blackpool.

STARK, H. W., M.B. Edin.: senior hospital M.O. in anæsthetics, Stornoway hospitals.

* TRAFFORD, H. S., M.B. Manc., D.OBST., F.R.C.S.E.: senior casualty officer (S.H.M.O.), Stoke-on-Trent group of hospitals.

WARBOYS, J. W., M.D. Sheff., D.P.M.: whole-time senior asst. psychiatrist, Middlewood Hospital, Sheffield.

South-Western Regional Hospital Board:

JACKSON, E. G. A., B.SC., M.B. Wales, F.F.A.R.C.S., D.A.: anæsthetic registrar, Southmead Hospital, Bristol.

PYBUS, P. K., M.B. Camb., D.OBST.: surgical registrar, Torquay and Newton Abbot hospitals.

TUFMAN, G. S., B.SC., M.B. Manc., F.R.C.S.: senior registrar in orthopædic and traumatic surgery, Bath clinical area.

Appointed Factory Doctors:

LANG, H. A., M.B. Glasg.: Colmonell, Ayr.

REDMOND, D. S., M.B. Belf.: Hednesford, Stafford.

* Amended notice.

Diary of the Week

OCT. 18 TO 23

Monday, 18th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
3 P.M. Sir Charles Symonds: The Circle of Willis. (Harveian Oration.)

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Dr. J. Purdon Martin: Disorders of Ocular Movement of Nuclear and Supra-nuclear Origin.

HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Dr. W. S. C. Copeman: Twenty-five Years a Hunterian. (Presidential address.)

Tuesday, 19th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. B. E. Heard: Effect of Very Low Temperature on Living Tissue. (Erasmus Wilson demonstration.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (Senate House, University of London, W.C.1) Prof. A. V. Hill, F.R.S.: Why Biophysics?

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *Pathology.* Prof. L. P. Garrod: Chemicals versus Bacteria. (Presidential address.)

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Dr. Grantley Dick Read: Preparation for Labour.

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. E. J. Moynahan: Urticaria.

SOCIETY FOR THE STUDY OF ADDICTION
8 P.M. (Medical Society of London, 11, Chandos Street, W.1.) Dr. J. S. Heller: Pathological Changes Produced by Excessive Consumption of Alcohol.

Wednesday, 20th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
2 P.M. Dr. H. Harris: Biochemical Genetics.

ROYAL SOCIETY OF MEDICINE
5 P.M. *Comparative Medicine.* Sir Weldon Dalrymple-Champneys: Non-specific Physiological Factors Controlling the Phenomena of Parasitism. (Presidential address.)
8.15 P.M. *General Practice.* Dr. A. Talbot Rogers: General Practice in Review. Valedictory address.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. Haber: Diagnosis by Biopsy and Cytology.

EUGENICS SOCIETY
5.30 P.M. (Royal Society, Burlington House, Piccadilly, W.1.) Prof. S. Chandrasekhar: Infant Mortality in India: 1901–1951. A Demographic Revolution.

Thursday, 21st

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. A. G. Riddell: Ammonia Intoxication in Surgical Patients. (Arris and Gale lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. B. S. Platt: Protein Malnutrition.

ROYAL SOCIETY OF MEDICINE
4.45 P.M. *Dermatology.* Demonstration of cases.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
5 P.M. Dr. Frankis T. Evans: Veins and the Anæsthetist. (Bengué Memorial Award lecture.)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. R. B. Heisch (Kenya): Epidemiology of Kala-azar in Kenya.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
7.30 P.M. (Rembrandt Hotel, Thurloe Place, S.W.7.) Dr. W. R. Thrower: Journey from the Bench to the Bedside. (Presidential address.)

MEDICAL RESEARCH COUNCIL, National Institute for Medical Research, The Ridgeway, Mill Hill, N.W.7
5 P.M. Dr. J. H. Hanks (Harvard): Application of Metabolic Study to Leprosy Research.

Friday, 22nd

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Brigadier-General Sam F. Seeley (U.S. Army): Advances in the Management of War Wounds of the Vascular System.

ROYAL SOCIETY OF MEDICINE
8.15 P.M. *Obstetrics and Gynæcology.* Mr. Frederick Roques: Pregnancy Complicated by Tumours. (Presidential address.)

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. J. Wallace: Clinical Demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330–332, Gray's Inn Road, W.C.1
3.30 P.M. Mr. Anthony Radcliffe: Nasal Obstruction and Nasal Catarrh.

MEDICAL SOCIETY FOR THE CARE OF THE ELDERLY
10 A.M. (General Hospital, Sunderland.) Opening of two-day meeting.

BRITISH ASSOCIATION OF ALLERGISTS
5 P.M. (St. Mary's Hospital, Paddington, W.2.) Opening of two-day meeting.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, Vincent Street, Glasgow, C.2
5 P.M. Prof. W. Arthur Mackey: Indications for Surgery in Heart-disease.

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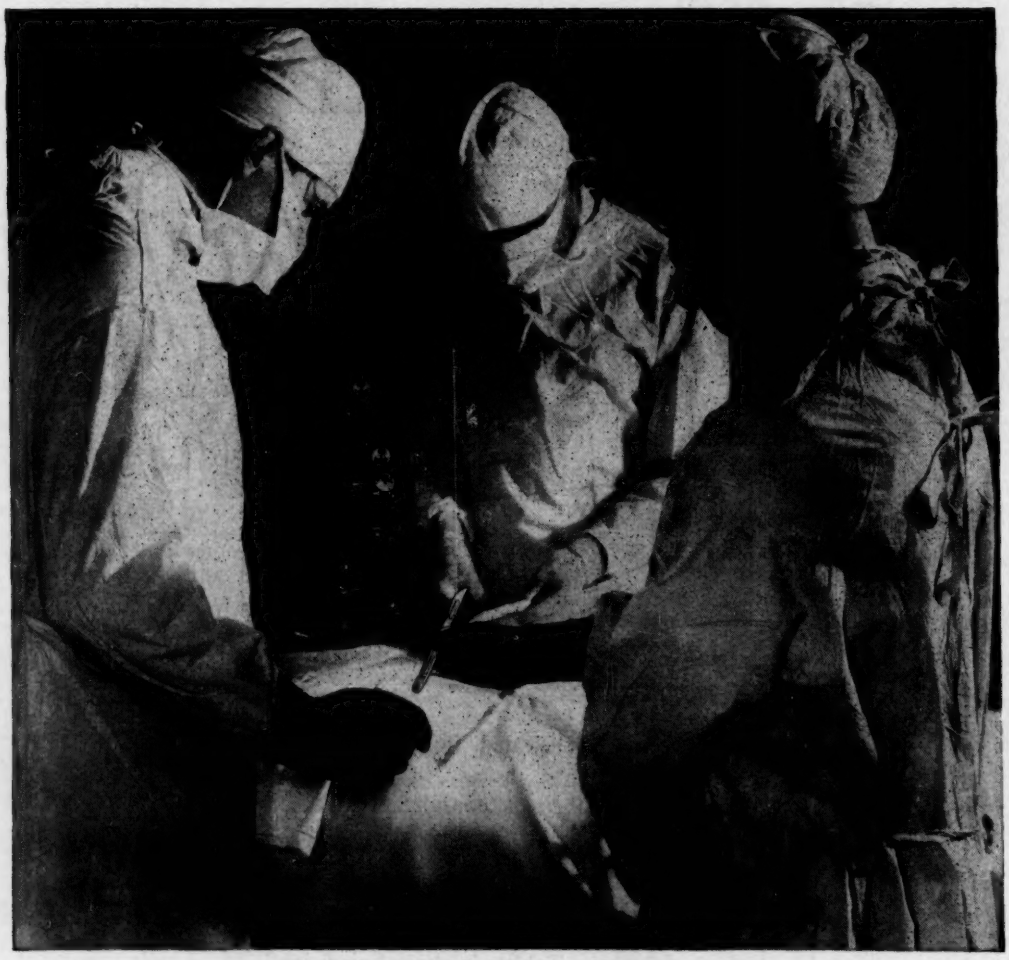

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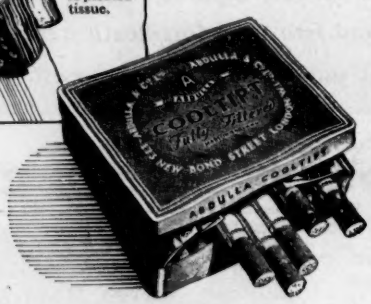

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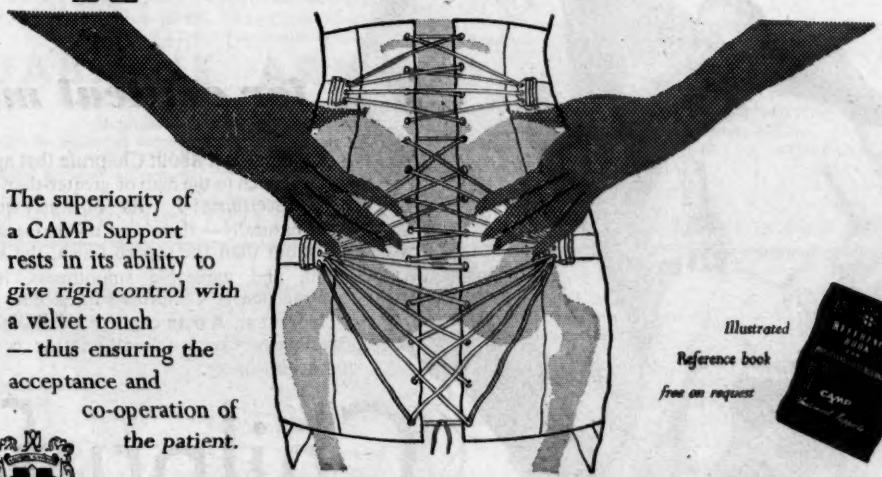

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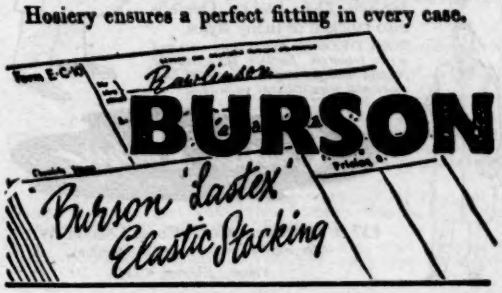

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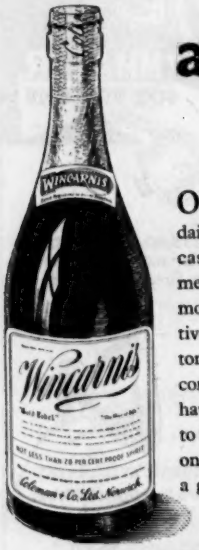

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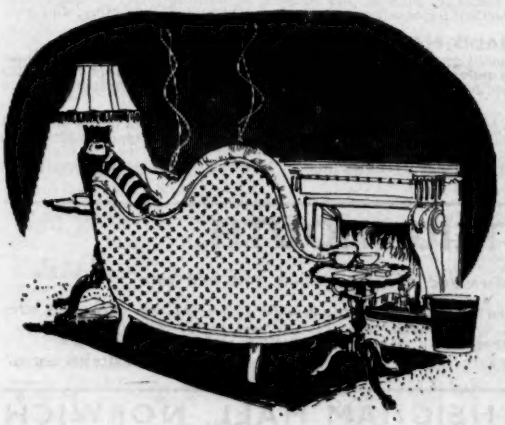

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MACEWEN MEMORIAL LECTURE

The Macewen Memorial Lecture will be delivered by REYNALDO DOS SANTOS (Emeritus Professor of Surgery in the University of Lisbon) in the Lecture Theatre, Chemistry Building, on MONDAY, 18TH OCTOBER, 1954, at NOON.

Subject: "The Present and Future of Arteriography."

The Lecture is free and open without ticket to Members of the University and to the Public.

INSTITUTE OF ORTHOPÆDICS

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL,
234, Great Portland-street, W.1
(UNIVERSITY OF LONDON)

COURSE ON DISORDERS OF JOINTS
15TH–20TH NOVEMBER
Provisional Programme Below

Fractures into joints (L)	Mr. P. H. NEWMAN
Manipulation of joints (D)	Mr. H. J. BURROWS
Arthrodesis Arthroplasty (L/D) ..	Mr. K. I. NISSEN
Internal Derangement of knee (LD) ..	Mr. R. Y. PATON
Ankylosing Spondylitis (LD)	Prof. B. W. WINDEYER
Rheumatoid arthritis (LD)	Dr. R. NASSIM
C.D.H. (D)	Mr. D. TREVOR
Dislocations (L)	Mr. H. J. BURROWS
Tuberculosis of spine (D)	Mr. H. J. SEDDON
Tuberculosis of hip and knee (D) ..	Mr. J. A. CHOLMELEY
The Pathology of Joint Diseases (LD) ..	Dr. H. A. SISSONS
Hallux valgus and rigidus (LD) ..	Mr. G. L. W. BONNEY
Loose bodies in joints (L)	Mr. A. W. L. KESSEL
Septic arthritis	Mr. K. I. NISSEN
Chemistry of synovial fluid (LD) ..	Dr. P. G. WALKER
Ætiology and treatment of contractures (LD) ..	Mr. J. I. P. JAMES Mr. R. L. G. DAWSON
Bacteriology of joint disease (LD) ..	Dr. C. H. LACK
General Management of joint tuberculosis (LD) ..	Dr. F. H. STEVENSON
Spondylolisthesis (LD)	Mr. P. H. NEWMAN
Intervertebral disc lesions (LD) ..	Mr. V. LOGUE

The fee for this course (including lunch and tea) is 7 guineas.

Early application should be made to the Dean at 234, Great Portland-street, W.1.

THE LONDON HOSPITAL MEDICAL COLLEGE

COURSE IN ADVANCED MEDICINE

A *Postgraduate Course in Medicine* will be held at The London Hospital commencing MONDAY, 10TH JANUARY, and finishing FRIDAY, 18TH MARCH, 1955. Classes will be held on Mondays, Wednesdays and Fridays. The course will be limited to 24 students.

Applications should be made to the Dean. The fee for the whole course will be 35 guineas, and for Old Londoners 15 guineas.

H. B. MAY, M.A., M.D., M.R.C.P., Dean.

Turner-street, London, E.1.

THE ROYAL SOCIETY

GOVERNMENT GRANT FOR SCIENTIFIC INVESTIGATIONS

Applications for grants from the third allotment of the Government Grant for Scientific Investigations for the year 1954 should be made as soon as possible on forms of application to be obtained from the Assistant Secretary of the Royal Society, Burlington House, London, W.1. No application can be considered which is received later than 20TH NOVEMBER, 1954.

Applicants must be of British nationality, resident in Great Britain or Northern Ireland. Grants may be made for purposes in connection with the promotion and support of research in pure science other than for personal maintenance or payment of stipends; for the assistance of scientific expeditions and collections; but not in aid of scientific publications.

UNIVERSITY COLLEGE OF THE WEST INDIES.

Applications are invited for SENIOR LECTURESHIP IN MEDICINE. Duties will include assistance to the Professor of Medicine in teaching students for medical degrees of University of London, care of patients in the University College Hospital and research in the Department of Medicine. Salary scale is £1300–£50–£1800 p.a.; point of entry determined by qualifications and experience. Child allowance. F.S.S.U. Unfurnished accommodation at rental of 5% of basic salary. The successful applicant will be expected to take up the post as early as possible in 1955.

Applications (10 copies), giving full particulars of qualifications and experience, and names of 3 referees, should be received before 22nd November, 1954, by Secretary, Senate Committee on Higher Education in the Colonies, University of London, W.C.1, from whom further particulars may be obtained.

BRITISH POSTGRADUATE MEDICAL FEDERATION.

(UNIVERSITY OF LONDON.) INSTITUTE OF CARDIOLOGY (associated with the National Heart Hospital, Westmorland-street, W.1). Applications are invited for the post of FIRST ASSISTANT to the Academic Unit, vacant as from 1st January, 1955. The successful candidate will have the status of a Senior or Junior Lecturer, salary scale either £1250–£100–£1450 or £900–£100–£1100 p.a., according to qualifications and experience. Superannuation under the F.S.S.U. The appointment is for 1 year in the first instance but may be extended annually up to a maximum of 5 years.

Applications, together with the names of 3 referees, should be sent to the Dean at 35, Wimpole-street, W.1, not later than 12th November, 1954.

Hospital Services: Senior Appointments

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) SENIOR CASUALTY OFFICER (whole-time) at Watford Peace Memorial Hospital, Watford (196 Beds), to organise the work of a busy Casualty Department and to act as Admissions Officer, subject to the general supervision of the Senior Surgeon of the department. A higher qualification in surgery is desirable. Duration of tenure of post not exceeding 4 years. Salary scale £1500 (unless below age 32)–£1950. Successful candidate must reside near the Hospital.

Applications by 18th November, 1954.

(2) ASSISTANT PHYSICIAN in Physical Medicine (whole-time), Edgware General Hospital, Edgware, Middlesex (651 Beds). Salary scale £1500 (unless below age 32)–£1950.

Applications by 16th November, 1954.

(3) CONSULTANT in Morbid Anatomy (whole-time) at North Western Group Laboratory, 4–8, Pond-street, N.W.3, to undertake the morbid anatomy and histology of Paddington General Hospital, W.9 (564 Beds), and St. Charles' Hospital, W.10 (593 Beds).

Applications by 24th November, 1954.

(4) CONSULTANT OPHTHALMOLOGIST (part-time) for 1 half-day a week at Royal London Homœopathic Hospital, W.C.1 (183 Beds).

Applications by 29th November, 1954.

Hospitals and Laboratory may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

ROYAL MASONIC HOSPITAL, Ravenscourt Park, London, W.6. Applications are invited from Fellows of 1 of the Royal Colleges of Surgeons for the appointment of CONSULTANT SURGEON at the above Hospital as from 1st April, 1955. Candidates must be engaged in consulting practice and well established in their profession.

Applications, giving detailed information, and the names and addresses of 3 referees, should reach the undersigned (from whom further information may be obtained) on or before 30th November, 1954.

R. E. LAWSON, Secretary and House Governor.

BATH CLINICAL AREA. South-Western Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the appointment of ASSISTANT PSYCHIATRIST at Mendip Hospital, Wells, which contains approximately 970 Beds. The appointment will be on a whole-time basis in the Senior Hospital Medical Officer grade. Applicants should possess the Diploma in Psychological Medicine, and previous experience of the diagnosis and treatment of mental diseases is essential. The successful candidate will work under the general direction of the Physician-Superintendent of Mendip Hospital. An unfurnished house is available.

Applications (12 copies), stating date of birth, qualifications and experience, together with 12 copies of 2 testimonials, and the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 30th October, 1954.

DARTFORD HOSPITAL MANAGEMENT COMMITTEE. Locum CONSULTANT ANÆSTHETIST required for 9 sessions a week in the Dartford Group of hospitals from 29th October, 1954.

Applications to the Group Secretary, The Bow Arrow Hospital, Dartford, Kent.

EXETER CLINICAL AREA. South-Western Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the appointment of a CONSULTANT SURGEON in the Exeter Clinical Area which comprises Exeter, Torquay, North and East Devon. The appointment may be held either on a whole-time or maximal (9 sessions) part-time basis. The successful candidate will have charge of beds at the Royal Devon and Exeter Hospital, Exeter, and at the Exeter City Hospital, and will be required to visit other hospitals in the Clinical Area as may be determined by the Regional Board from time to time.

Applications (12 copies), stating date of birth, qualifications and experience, together with 12 copies of 2 testimonials, and the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 6th November, 1954.

ST. HELENS. PROVIDENCE HOSPITAL. Applications invited for post of HONORARY CONSULTANT GYNÆCOLOGIST at above Hospital. The Hospital has 125 Beds and an Outpatients Department and the appointment will be for 2 notional half-days per week exclusive of emergencies.

Applications, giving full details of qualifications and experience, and names and addresses of 2 referees, should be forwarded to undersigned not later than 30th October, 1954.

WILLIAM I. LIVESEY, Honorary Secretary.
Providence Hospital, St. Helens.

MANCHESTER REGIONAL HOSPITAL BOARD.

(a) 2 whole-time resident posts of CONSULTANT PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT to :—

(i) Whittingham Hospital, near Preston (about 3000 Beds).

(ii) Lancaster Moor Hospital, near Lancaster (about 2500 Beds).

All modern forms of treatment undertaken. Wide experience in psychiatry essential. Very good residential accommodation available. Further inquiries to be made of respective Medical Superintendents. 26th October, 1954.

(*b*) Part-time (8 half-days) post of CONSULTANT E.N.T. SURGEON to the Lancaster and Kendal Hospital Centre (Royal Lancaster Infirmary, Queen Victoria Hospital, Morecambe, and Westmorland County Hospital, Kendal, &c.). An E.N.T. Unit of 20 Beds, with new theatre is being provided at Beaumont Hospital, Lancaster, and there will also be duties at Kendal and Morecambe. Wide experience and higher qualifications essential. Appointee to live in area. 1st November, 1954.

Application forms from the Senior Administrative Medical Officer to the Board at Cheetwood-road, Manchester, 8, to be returned by dates stated.

PLYMOUTH CLINICAL AREA. South-Western Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the appointment of a CONSULTANT *OPHTHALMOLOGIST in the Plymouth Clinical Area* which comprises Plymouth, Kingsbridge, Tavistock, Launceston, Bude and Liskeard. The appointment may be held either on a whole-time or maximal (9 sessions) part-time basis. Applicants should have had wide experience in ophthalmology. The successful candidate will have charge of beds at Plymouth Royal Eye Infirmary, and will be required to visit other hospitals in the Clinical Area as may be determined by the Regional Board from time to time.

Applications (12 copies), stating date of birth, qualifications, and experience, together with 12 copies of 2 testimonials, and the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 6th November, 1954.

Applications are also invited to undertake the work on a locum basis until the permanent appointment is made.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. Applications are invited for an appointment of Whole-time ANÆSTHETIST of Consultant grade for duty in the Regional Pool of Anæsthetists based on the Royal Infirmary of Edinburgh. Experience in the administration of anæsthetics for thoracic surgery is essential. The post is superannuable and the conditions of service are in accordance with the regulations.

Applications, giving particulars of age, qualifications and experience, together with the names of 3 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, *Drumsheugh-gardens*, Edinburgh, 3, by 6th November.

SHEFFIELD REGIONAL HOSPITAL BOARD. Con-SULTANT ORTHOPÆDIC SURGEON required for 8 notional half-days per week. Main Centre Grimsby, with other duties at Scunthorpe or Louth.

Further details and application forms from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10. To arrive not later than 6th November, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Con-SULTANT OBSTETRICIAN AND GYNÆCOLOGIST required for 7 notional half-days per week. The successful candidate will have charge of gynæcological beds at the Scunthorpe and District War Memorial Hospital and the Glandford Hospital, Brigg ; and obstetrical beds at the Scunthorpe Maternity Home.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10. Forms to be returned by 13th November, 1954.

SOUTH EAST METROPOLITAN REGIONAL HOS-PITAL BOARD. Applications are invited for an appointment as Part-time CONSULTANT PSYCHIATRIST to undertake 4 notional half-days a week for child guidance work at the Hastings Child Guidance Clinic, 33, Cambridge-road, Hastings, Sussex, which is administered by the East Sussex County Council. Candidates must have had previous extensive experience of child guidance. Possession of a D.P.M. is essential and preferably a higher qualification. Applicants may visit the Clinic.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, by 30th October, 1954.

WESTERN AUSTRALIA. PRINCESS MARGARET HOSPITAL FOR CHILDREN, PERTH, WESTERN AUSTRALIA. The Board of Management invites inquiries from qualified medical practitioners for the whole-time post of PATHOLOGIST. Intending candidates must have previous experience and furnish details of higher qualifications. Salary £2500 (Australian) p.a.—subject to cost-of-living adjustments. Reasonable travelling expenses allowed if appointee enters into bond to serve for a minimum of 2 years.

Inquiries as to further general and medical detail should be addressed, by air mail, to J. D. CLARKSON, Manager.

CANADA. REGINA GENERAL HOSPITAL, Regina, SASKATCHEWAN. Applications are invited for a CLINICAL PATHOLOGIST (800-Bed General Hospital). General Pathology Department with a Director, and an Assistant Pathologist already on staff. Emphasis to be placed on hæmatology and bacteriology. Salary and conditions of employment by agreement. Minimum starting salary $6000.

Applications to be forwarded to Superintendent, Regina General Hospital, Regina, Saskatchewan.

CANADA. REGINA GENERAL HOSPITAL, Regina, SASKATCHEWAN. Applications are invited for a RADIOLOGIST (800-Bed General Hospital). General Radiographic Service, mostly diagnostic. Remuneration and conditions of service to be arranged. Minimum starting salary $8000.

Applications to be forwarded to Superintendent, Regina General Hospital, Regina, Saskatchewan.

NEW ZEALAND. COOK HOSPITAL BOARD, Gisborne, NEW ZEALAND. Applications, closing Friday, 19th November, 1954, are invited from registered medical practitioners for the appointment of Full-time ANÆSTHETIST. Salary in accordance with the Hospital Employment Regulations. Salary rate for the following gradings :—

Senior Registrar £1048 *5s.*–£1163 *5s.*

Junior Specialist £1352 12s.–£1652 12s.

Amounts quoted are in New Zealand currency. The position is non-resident. Gisborne, with a population of 21,000 is situated on the sea coast, and enjoys an ideal climate.

Conditions of appointment will be supplied on application to the High Commissioner for New Zealand, 415, Strand, London, W.C.2, quoting reference No. A 3/65/10 and mentioning this paper. Applications to be sent direct to the Secretary, Cook Hospital Board, Gisborne, New Zealand.

Hospital Services : Junior Appointments

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE PHYSICIAN (resident), vacant 4th November, 1954. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 25th October, 1954.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. Locum ORTHOPÆDIC REGISTRAR (Senior or middle grade) required for 2 months commencing immediately.

Apply to Medical Director.

CHARING CROSS HOSPITAL, W.C.2. Senior House OFFICER in Pathology (part-time resident), for 1 year in the first instance with eligibility for renewal for 1 further year and promotion to Registrar grade.

Application forms, obtainable from the undersigned, to be returned by 25th October, 1954.

FRANK HART, Secretary to the Board.

CHARING CROSS HOSPITAL, W.C.2. Medical Registrar (*full-time*). Grade, Registrar or Senior Registrar, according to qualifications and experience. Tenable for 1 year in the first instance, with eligibility for renewal.

Application forms, obtainable from the undersigned, to be returned by 25th October, 1954.

FRANK HART, Secretary to the Board.

FOREST GATE HOSPITAL, Forest-lane, London, E.7. Pre-registration OBSTETRIC HOUSE OFFICER (second post) required for 6 months commencing 1st December, 1954. The appointment is recognised for the training of candidates for D.Obst.R.C.O.G.

Applications, with names of 2 referees, to the Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15 by 23rd October, 1954.

FRIERN HOSPITAL, New Southgate, London, N.11. (2470 Beds.) PSYCHIATRIC REGISTRAR required at above Hospital. Candidates should have adequate general medical and psychiatric experience. Details of the appointment and work in the Hospital may be obtained on application to the Physician-Superintendent and applicants are invited to visit the Hospital by appointment.

Application forms obtainable from, and returnable to, Secretary, Friern Hospital, within 14 days.

HACKNEY HOSPITAL, London, E.9. (General—644 Beds.) Applications from registered medical practitioners for the posts of HOUSE OFFICERS (third post—casualty) (1 with additional duties in the Skin Department and 1 with additional duties in the E.N.T. Department), should be sent as soon as possible to the Group Secretary at the above address.

HOSPITAL FOR TROPICAL DISEASES, 4, St. Pancras-way, N.W.1. (UNIVERSITY COLLEGE HOSPITAL.) Applications are invited for the post of SENIOR REGISTRAR in Tropical Medicine (non-resident).

Applications, with names of 2 referees, to the Administrator and Secretary, University College Hospital, Gower-street, W.C.1, by 12th November, 1954.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. Applications are invited for the appointment of RESIDENT MEDICAL OFFICER. Appointment for 1 year from 1st January, 1955, and graded as Registrar.

Applications, stating age, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should be sent to the undersigned not later than 13th November, 1954. THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON JEWISH HOSPITAL, Stepney Green, E.1. (130 Beds.) HOUSE SURGEON (pre-registration or first, second, or third) required for 6 months commencing 5th November, 1954.

Applications, with copies of testimonials, to be sent to the Hospital Secretary.

MEMORIAL HOSPITAL, Woolwich, S.E.18. Casualty OFFICER, vacant 17th November. 6 months appointment, recognised for F.R.C.S. Senior House Officer grade, salary £745 p.a., less £150 p.a. for residence.

Apply to Secretary.

MILE END HOSPITAL, Bancroft-road, E.1. (475 Beds.) HOUSE PHYSICIAN (pre-registration or first, second, or third) required for 6 months commencing 18th November, 1954.

Application forms obtainable from Physician-Superintendent, to be returned by 23rd October with copies of not more than 3 testimonials.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited for appointment of RESIDENT CASUALTY OFFICER at above Hospital from 8th November, 1954. Senior House Officer grade. Recognised for the F.R.C.S.

Forms of application from the Physician-Superintendent.

LONDON HOSPITAL AND THE NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR to the Department of Anæsthetics. Candidates must hold a higher degree in anæsthetics. The appointment will be for 4 years to be spent at the following hospitals :—

First year The London Hospital.
Second year at a Regional Hospital.
Third year St. Bartholomew's Hospital.
Fourth year at 1 of the above by arrangement.

Applications (12 copies), giving the names and addresses of 3 referees, should be received by the House Governor by 3rd November, 1954. H. BRIERLEY, House Governor.

NATIONAL HEART HOSPITAL, Westmoreland-street, W.1. (With which is associated The Institute of Cardiology.) The Board of Governors invites applications to fill a vacancy in the post of SENIOR REGISTRAR as from 1st January, 1955. Applicants should have been fully trained in general medicine and should possess a higher medical qualification. Opportunities for research are available.

Applications, with copies of 3 recent testimonials, should be sent to me not later than Saturday, 23rd October, 1954.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON at The National Hospital, Queen-square, W.C.1, commencing 1st February, 1955. This post carries the grade of Registrar.

Applications, giving the names of 3 referees, to be sent to the undersigned not later than 30th October, 1954.

H. EWART MITCHELL,
Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, W.C.1.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited for the post of RESIDENT MEDICAL OFFICER (or if the present House Physician is appointed to this post there will be a vacancy for House Physician) at Maida Vale Hospital for Nervous Diseases, London, W.9. Appointment in the first instance for 6 months from 1st November. Grading as Senior House Officer or Registrar according to experience. Preference will be given to a candidate holding a higher degree and previous neurological experience will be an asset.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, at Maida Vale Hospital, not later than 23rd October, 1954.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD AND BOARD OF GOVERNORS OF ST. BARTHOLOMEW'S HOSPITAL.

SENIOR REGISTRAR—Diseases of the Chest. The appointment will be held for 2 years at Broomfield Hospital, near Chelmsford, with visits to St. Bartholomew's Hospital, E.C.1, and for 2 years at Lancaster House Chest Clinic, Southend.

The post is resident at Broomfield Hospital, which has 335 Beds with Tuberculous and Non-tuberculous Thoracic Surgery Unit, Outpatient Clinics, and Mass Radiography Unit.

The post is resident or non-resident at Lancaster House Chest Clinic and there is single accommodation available in the Group. Duties are chiefly at Lancaster House Chest Clinic and include the care of 30 patients with pulmonary tuberculosis and a few beds for diagnosis at Westcliff Hospital.

Appointment subject to annual review.

Applications in triplicate, with names of 2 referees, to Secretary, North East Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 30th October, 1954.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) REGISTRAR in Diseases of the Chest (resident), Broomfield Hospital, near Chelmsford. Will assist in theatre, and relief duties will involve care of pre- and post-operative tuberculous and non-tuberculous thoracic surgery cases.

(2) REGISTRAR in Diseases of the Chest (resident), High Wood Hospital for Children, Brentwood, Essex. Experience in tuberculosis or diseases in childhood essential.

(3) REGISTRAR in Diseases of the Chest (resident), Harts Hospital, Woodford Green Essex. Post offers exceptional opportunities for experience in tuberculosis and diseases of the chest. The Hospital includes Area Chest Clinic and Thoracic Surgical Unit and is easily accessible to central London by tube or bus.

(4) MEDICAL REGISTRAR (resident), St. John's and Chelmsford and Essex Hospitals. Post recognised for D.C.H. Some duties in Group Pædiatric, Premature Baby and Neonatal Departments.

(5) SURGICAL REGISTRAR (resident), Poplar Hospital, East India Dock-road, E.14. Candidates should hold F.R.C.S.

(6) ANÆSTHETIC REGISTRAR (resident), Chelmsford and Essex and St. John's Hospitals. Recognised for D.A.

(7) *ANÆSTHETIC REGISTRAR (resident or non-resident),* St. Andrew's Hospital, Billericay, Essex.

(8) REGISTRAR in Mental Deficiency (resident or non-resident). (House available if required.) Royal Eastern Counties Hospital, Colchester, Essex. Recognised for D.P.M.

(9) E.N.T. REGISTRAR (resident or non-resident), General Hospital, Southend-on-Sea, Essex. Post vacant in early December. Recognised for D.L.O. of Conjoint Board and for F.R.C.S.

Appointments subject to review after 1 year.

Separate applications in duplicate with 2 copies of 2 recent testimonials to Secretary, 11A, Portland-place, W.1, by 30th October, 1954.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. 2 RESIDENT HOUSE PHYSICIANS (post-registration) required for 1st December, for 6 months. General medicine.

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials, to Secretary of Hospital, by 26th October.

PRINCESS BEATRICE HOSPITAL, Earls Court, S.W.5. REGISTRAR (general medicine). 3 half-days per week, Tuesday A.M. and P.M., Friday P.M. Vacancy 1st February, 1955.

Application forms from Group Secretary, St. Luke's Hospital, Chelsea, S.W.3. Enclose foolscap stamped addressed envelope.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. Applications are invited from candidates holding their M.R.C.O.G. for a full-time or a part-time post of SENIOR REGISTRAR in the service of the Board of Governors of this Teaching Hospital Group which will become vacant on 1st January, 1955. The successful applicant will be required to undertake duties at Queen Charlotte's Maternity Hospital and Chelsea Hospital for Women.

Applications, stating age, qualifications with dates, and previous appointments, together with the names of 3 referees, should be sent to the Secretary, 339, Goldhawk-road, London, W.6, not later than 31st October, 1954.

ROYAL FREE HOSPITAL. Applications are invited for the appointment of SENIOR REGISTRAR to the Orthopædic Department. Applicants must be registered medical practitioners and Fellows of the Royal College of Surgeons. The appointment is recognised under the Senior Registrar establishment and is for 1 year in the first instance. Duties to commence on 1st January, 1955.

Applications, together with the names of 3 referees, should be sent to the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 22nd October, 1954.

ROYAL FREE HOSPITAL. Applications are invited for the post of SENIOR SURGICAL REGISTRAR at the above Hospital. Candidates should be registered medical practitioners and Fellows of the Royal College of Surgeons. The appointment is recognised under the Senior Registrar establishment and is for 1 year in the first instance. Duties to commence on 1st January, 1955.

Applications, together with the names of 3 referees, should be sent to the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, not later than 22nd October, 1954.

ROYAL FREE HOSPITAL. Applications are invited from registered Men and Women medical practitioners for the appointment of RESIDENT ASSISTANT PATHOLOGIST at the above Hospital. Salary in accordance with Ministry of Health scale for House Officers. The appointment is for 6 months in the first instance, subject to possible reappointment for a further 6 months. Duties to commence on 1st January, 1955.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 29th October, 1954.

ROYAL MASONIC HOSPITAL, Ravenscourt Park, W.6. The post of RESIDENT SURGICAL REGISTRAR will become vacant about 15th November, 1954. Gross salary £850 (residential emoluments of £130 deductable).

Applications should state age, qualifications, past and present appointments, include 2 recent testimonials, and the names of 2 referees, and should reach the Hospital as soon as possible, but not later than first post on 21st October, addressed to the Secretary and House Governor, from whom further information would be given on request.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1. There will be a vacancy for an ANÆSTHETIC REGISTRAR (resident or non-resident) as from 20th December, 1954, to work as required at both hospitals. Applicants should have had some special experience in anæsthesia and preferably should hold, or be working for, a higher qualification in that specialty. Registrar grading and salary in accordance with the terms and conditions of service under the National Health Service Act.

Applications, giving full particulars of age, qualifications and experience, with the names of 2 referees, should be sent to the House Governor by 8th November, 1954.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1. RESIDENT HOUSE SURGEON (second or subsequent post). There will be a vacancy on 1st November, 1954. 6 months appointment, with salary as laid down for House Officer grades in the terms and conditions of service under the National Health Service.

Applications, stating age, qualifications, full details of previous experience (particularly in this specialty), with copies of 1–3 recent testimonials, should reach the House Governor by 26th October, 1954.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL AND THE INSTITUTE OF LARYNGOLOGY AND OTOLOGY, Gray's Inn-road, W.C.1, and Golden-square, W.1. Applications are invited for a post of REGISTRAR or alternatively SENIOR HOUSE OFFICER—a higher surgical qualification is required for the former grading and at least the Primary F.R.C.S. for the latter. Considerable clinical experience in general surgery and in this specialty is required for either post. The appointment will be in accordance with the terms and conditions of service for the appropriate grade in the National Health Service.

Applications, giving full information and the names of 2 referees, should be sent to the House Governor without delay.

ST. THOMAS'S HOSPITAL, London, S.E.1. Registrar to the Children's Department for a period of 1 year in the first instance.

Applications, including names and addresses of 2 referees, to the Clerk of the Governors by 31st October.

ROYAL NORTHERN HOSPITAL, Holloway, London, N.7. (279 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required in the Orthopædic and Fracture Department of the above Hospital. Candidates may visit the Hospital by direct appointment.

Application forms obtainable from, and returnable to, the Secretary, Royal Northern Hospital, N.7, by 26th October, 1954.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Camberwell Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th October, 1954.

ST. CHARLES' HOSPITAL, Ladbroke-grove, W.10. (593 Beds.) Applications are invited for the post of HOUSE PHYSICIAN (pædiatrics), commencing 1st November, 1954.

Applications, stating age, qualifications, experience, together with names and addresses of 2 referees, to Hospital Secretary immediately.

ST. JAMES' HOSPITAL, Sarsfeld-road, Balham, S.W.12. WANDSWORTH HOSPITAL GROUP. HOUSE PHYSICIAN (pædiatrics) required.

Applications, stating age, qualifications, experience, and names of 2 referees, to Group Secretary, at the above address, immediately.

ST. JAMES' HOSPITAL, Sarsfeld-road, S.W.12. Wandsworth Hospital Group. SENIOR HOUSE OFFICER (casualty) required November.

Applications, full details, and names of 2 referees, to Group Secretary by 25th October.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (General—182 Beds.) Applications are invited from registered or provisionally registered practitioners for the post of HOUSE PHYSICIAN for 6 months commencing 1st December, 1954.

Applications, with 2 recent testimonials, to Hospital Secretary by 30th October, 1954.

ST. MARY'S HOSPITAL, W.2. Applications are invited from suitably qualified practitioners for the post of CASUALTY SURGEON (resident). Candidates must have held an appointment as House Surgeon at this Hospital or at another hospital approved by the Board of Governors. The appointment is for a first period of 6 months, with effect from 1st January, 1955; remuneration at Senior House Officer rate.

Applications, stating nationality, date of birth, permanent address, qualifications, with dates and details of present and previous appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 27th October, 1954.

ST. MARY'S HOSPITAL, W.2. Applications are invited from suitably qualified registered practitioners for the post of RESIDENT ANÆSTHETIST. The appointment is for a first period of 6 months, and the successful candidate will be required to take up his duties on 3rd January, 1955, at a salary of £525, less £125 p.a. for board and residence provided.

Applications, stating nationality, date of birth, permanent address, qualifications with dates and experience, together with names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, by 27th October, 1954.

ST. MARY'S HOSPITAL, London, W.2 (Ophthalmic DEPARTMENT); WESTERN OPHTHALMIC HOSPITAL, Marylebone-road, N.W.1. Applications are invited for the post of Whole-time SENIOR REGISTRAR (non-resident). Candidates must have postgraduate experience and should hold, or be studying for, the F.R.C.S. The successful candidate will be expected to take up his duties as soon as possible.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, and details of previous and present appointments and experience, together with the names and addresses of 3 referees, should reach the undersigned by 26th October, 1954.

ALAN POWDITCH, Secretary to the Board of Governors.

ST. MARY'S HOSPITAL, Paddington, W.2, and THE NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRARS in General Surgery (2 vacancies) required on 1st January, 1955, for a combined appointment which will normally be for a period of 4 years—namely, first and fourth years at St. Mary's Hospital; second and third years at Ashford and Paddington Hospitals. Possession of higher surgical qualifications essential. Hospitals may be visited by direct appointment.

Applications, stating nationality, date of birth, permanent address, qualifications with dates and details of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 27th October, 1954.

ST. MARY'S HOSPITAL, Paddington, W.2, and THE NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in General Medicine required on 1st January, 1955, for a combined appointment which will normally be for a period of 4 years—namely, first and fourth years at St. Mary's Hospital; second and third years at West Middlesex Hospital. Possession of higher medical qualification essential. Hospitals may be visited by direct appointment.

Applications, stating nationality, date of birth, permanent address, qualifications with dates and details of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 27th October, 1954.

ST. NICHOLAS HOSPITAL, Plumstead, London, S.E.18. CASUALTY OFFICER, vacant 1st November. Recognised for F.R.C.S. 6 months appointment (not pre-registration). Salary £525 p.a., less £125 p.a. for residence. There is also a Senior House Officer in the department.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy for a Whole-time ASSISTANT MEDICAL REGISTRAR (Registrar grade), falling vacant immediately.

Further particulars and form of application, which must be returned not later than Monday, 1st November, 1954, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of ASSISTANT BACTERIOLOGIST (graded Junior Hospital Medical Officer) in the Department of Clinical Pathology from 1st January, 1955. Candidates should have some experience in pathology.

Applications, with names of 2 referees, to Administrator and Secretary by 29th October, 1954.

WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone (NO. 10) HOSPITAL GROUP. Applications are invited for the post of HOUSE SURGEON (pre-registration post) in General Surgery at above Hospital, which falls vacant on 1st December, 1954.

Application forms from the Hospital Secretary to be returned within 14 days of the appearance of this advertisement.

WHITTINGTON HOSPITAL, Highgate Hill, N.19. Locum Tenens ORTHOPÆDIC REGISTRAR required for 2 months, from 4th November, 1954.

Applications to Medical Superintendent. (Tel.: ARChway 3070).

ALTON, HAMPSHIRE. LORD MAYOR TRELOAR ORTHOPÆDIC HOSPITAL. Applications are invited from registered medical practitioners for the post of Whole-time ORTHOPÆDIC REGISTRAR. Post provides experience in non-pulmonary tuberculosis and general orthopædics and includes attendances at peripheral clinics. Accommodation available. Canvassing disqualifies, but visit to Hospital welcomed.

Write to Secretary for application form.

ALTON, HAMPSHIRE. LORD MAYOR TRELOAR ORTHOPÆDIC HOSPITAL. LOCUM for Orthopædic Registrar required immediately at the above Hospital for 3 months. Good surgical experience required. Post provides experience in non-pulmonary tuberculosis and general orthopædics and includes attendances at peripheral clinics. Salary £16 per week, less emoluments.

Apply at once, with names of 2 referees, to the Secretary, Lord Mayor Treloar Orthopædic Hospital, Alton, Hants.

AYLESBURY, BUCKINGHAMSHIRE. ROYAL BUCKINGHAMSHIRE HOSPITAL. HOUSE SURGEON to the Department of Ophthalmology which is centred on this Hospital and which conducts work at peripheral clinics. Vacant now. Post is recognised for D.O. and duties will include some childrens surgery.

Applications, with 2 testimonials, to Secretary-Superintendent as soon as possible.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

RESIDENT ANÆSTHETIST (Senior House Officer grade). Main duties at Bolton District General Hospital and Bolton Royal Infirmary. Vacant 21st October, tenable for 12 months and recognised for the D.A.

Bolton District General Hospital (604 Beds)

RESIDENT HOUSE SURGEON for general surgical duties, vacant 22nd October, tenable for 6 months and recognised under the Pre-registration Service Scheme. Also recognised for F.R.C.S.

RESIDENT HOUSE PHYSICIAN, vacant 9th November, tenable for 6 months and recognised under the Pre-registration Service Scheme.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BARNSLEY. BECKETT HOSPITAL. (182 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SURGICAL REGISTRAR required. Single accommodation available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

BASINGSTOKE, HAMPSHIRE. PARK PREWETT GROUP HOSPITAL MANAGEMENT COMMITTEE, NO. 47. Registered medical practitioners are invited to apply for the appointments of PSYCHIATRIC REGISTRARS at Park Prewett Hospital, Basingstoke. Appointments will be vacant on 2nd and 5th January, 1955. The Hospital (1475 Beds), deals with all types of psychiatric illnesses and experience may be obtained in all modern physical, occupational and psycho-therapeutic methods.

Application forms in quintuplicate may be obtained from the Group Secretary upon receipt of a stamped addressed envelope, and must be returned within 14 days of the appearance of this advertisement.

BATH. ST. MARTIN'S HOSPITAL. Applications are invited from registered and pre-registered medical practitioners for 2 posts of HOUSE SURGEON at above Hospital which will become vacant during December.

Applications, stating age, qualifications, and experience, with 3 testimonials, should be forwarded to the undersigned by 23rd October, 1954. J. LAWRENCE MEARS, Secretary,

Bath Hospital Management Committee.

Manor Hospital, Bath.

BATH. ROYAL UNITED HOSPITAL. Applications are invited from registered and pre-registered medical practitioners for the post of HOUSE SURGEON at the above Hospital which becomes vacant at approximately the end of November.

Applications, stating age, qualifications, and experience, with 3 testimonials, should be forwarded to the undersigned by 23rd October, 1954. J. LAWRENCE MEARS, Secretary, Bath Hospital Management Committee.

Manor Hospital, Bath.

BATH. ROYAL NATIONAL HOSPITAL FOR RHEUMATIC DISEASES. Applications are invited from registered medical practitioners for the post of HOUSE PHYSICIAN (Senior House Officer grade) at the above Hospital attached to which is the Rheumatism Research Unit of South-Western and Oxford Regions. The Hospital is recognised for part 2 of the Diploma in Physical Medicine.

Applications, stating age, qualifications, and experience, with names of 2 referees, should be forwarded to the undersigned by 30th October, 1954. J. LAWRENCE MEARS, Secretary, Bath Hospital Management Committee.

Manor Hospital, Bath.

BEDFORD GENERAL HOSPITAL. (437 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for busy acute Orthopædic and Traumatic Department at above Hospital. Previous orthopædic experience desirable. Candidates may visit Hospital by appointment with the Group Secretary.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, as soon as possible.

BIRMINGHAM AND MIDLAND EYE HOSPITAL, Church-street, BIRMINGHAM, 3. HOUSE SURGEON required on 8th December. Appointment for 6 months, but renewable. Hospital carries resident staff of 5 and provides a 2-year course of instruction recognised for the D.O. (England) and F.R.C.S. (England) in Ophthalmology. Wide experience available in all branches, including surgery.

Detailed applications to Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. MONYHULL HALL HOSPITAL. (1142 Beds.) BIRMINGHAM (MENTAL D) GROUP OF HOSPITALS. Whole-time SENIOR REGISTRAR in Psychiatry, with some duties at ancillary premises, including residential special school for 350 children. Hospital recognised for D.P.M. Single accommodation available. Considerable experience specialty required. Successful candidate may subsequently be required to spend not more than 2 years in a selected hospital of the United Birmingham Hospitals in accordance with arrangements for the interchange of Registrars agreed between the 2 Boards.

Application forms from Secretary, Birmingham Regional Hospital Board, 10, Augustus-road, Birmingham, 15, to be returned before 1st November.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) Birmingham (Selly Oak) Hospital Management Committee, Oak Tree-lane, Birmingham, 29

Whole-time SURGICAL REGISTRAR for Birmingham Accident Hospital (209 Beds). Duties with accident surgery team and possibility of transfer to Burns Unit. General surgical experience essential. Higher qualification an advantage.

(2) South Warwickshire Hospital Group (No. 14), 50, Holly-walk, Leamington Spa

Whole-time REGISTRAR in Orthopædics. Duties mainly at Warwick Hospital (350 Beds, including 52 orthopædic). Recognised for F.R.C.S. Experience specialty essential and higher qualification an advantage.

Application forms from Group Secretaries, to be returned before 1st November, 1954. Candidates may visit Hospitals.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. YARDLEY GREEN HOSPITAL. THORACIC SURGICAL UNIT. Applications are invited for the post of SENIOR HOUSE OFFICER or HOUSE OFFICER according to experience. The appointment will give broad opportunities for experience in both tuberculous and non-tuberculous thoracic surgery.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Secretary, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM (SELLY OAK) GROUP 25 HOSPITAL MANAGEMENT COMMITTEE. Vacancy occurs for a SENIOR HOUSE OFFICER in Pathology in the main laboratory of this Group situated at Selly Oak Hospital. The post is a residential one and experience in hæmatology is an advantage but not essential. Salary in accordance with regulations.

Applications to the Pathologist, Selly Oak Hospital, Birmingham, 29.

BIRMINGHAM. ST. MARGARET'S HOSPITAL, Great BARR PARK, BIRMINGHAM, 22A. (Mental Deficiency Hospital.) Locum Tenens REGISTRAR required immediately (either sex). Salary £16 per week. Residential accommodation available.

Applications, stating names of 2 referees, to Medical Superintendent.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the non-resident post of SENIOR HOUSE OFFICER or REGISTRAR in Pædiatrics (grading according to experience) for duties at the Birmingham Maternity Hospital, Loveday-street, and the Maternity Department of the Queen Elizabeth Hospital. Previous experience, resident, in a Children's Hospital is essential, and candidates should hold the D.C.H. Post vacant immediately.

Applications, stating age, nationality, qualifications and previous appointments, should be forwarded to the House Governor, Birmingham and Midland Hospitals for Women, Showell Green-lane, Birmingham, 11, not later than 1st November, 1954.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL. HOUSE OFFICER (casualty) required to commence duty on 7th January, 1955, for 6 months. Recognised for pre-registration students, but registered practitioners may apply.

Forms of application may be obtained from the House Governor, The Children's Hospital, Ladywood-road, Birmingham, 16, and should be returned not later than 30th October, 1954. G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM AND MIDLAND HOSPITAL FOR WOMEN, Showell Green-lane, BIRMINGHAM, 11. Applications are invited from registered medical practitioners for the post of RESIDENT GYNÆCOLOGICAL HOUSE SURGEON (2 vacancies) occurring on 7th January, 1955. The posts are recognised for D.Obst.R.C.O.G. and M.R.C.O.G.

Application forms, obtainable from the House Governor at the above address, should be returned not later than 1st November, 1954. G. A. PHALP, Secretary.

BISHOP'S STORTFORD AND DISTRICT HOSPITAL, Rye-street, BISHOP'S STORTFORD, HERTS. (67 Beds—medical, surgical and maternity. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for a RESIDENT HOUSE OFFICER (not pre-registration). Appointment to commence as soon as possible.

Applications, stating age, nationality, qualifications and experience, with copies of recent testimonials or names of referees, should be sent to Hospital Secretary, Haymeads Hospital, Bishop's Stortford, Herts.

BLACKBURN. ROYAL INFIRMARY. (262 acute beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (surgery) required early in November at above Infirmary.

Apply to Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN. ROYAL INFIRMARY. (262 acute beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR (surgery) required early in November at above Infirmary. Recognised for F.R.C.S.

Apply to Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKPOOL. VICTORIA HOSPITAL. (344 Beds.) SENIOR HOUSE OFFICER (E.N.T. Department). Post vacant 1st December, 1954. Recognised for the F.R.C.S. and D.L.O.

Applications, with names and addresses of referees, to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (344 Beds.) RESIDENT HOUSE OFFICER (gynæcology and obstetrics). Recognised for M.R.C.O.G. Post vacant 1st November, 1954. This is a busy general hospital with a large Outpatient Department and the post offers excellent opportunities for experience under Consultant Gynæcologists and Obstetricians.

Applications, with names and addresses of referees, to the Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL. (492 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (resident), orthopædic and casualty combined. The post, which is recognised for the F.R.C.S. examination, becomes vacant on 27th October and is tenable for 12 months.

Applications to the Deputy Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. (492 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of 2 HOUSE PHYSICIANS, both posts vacant on 4th November and are recognised for pre-registration purposes.

Applications to the Deputy Hospital Secretary.

BRADFORD. ROYAL EYE AND EAR HOSPITAL. HOUSE SURGEON (ophthalmology), vacant 22nd November, 1954. Recognised for D.O.M.S. and F.R.C.S. Salary according to Whitley Council (MDB) rates.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRISTOL CLINICAL AREA. The Board of Governors of THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards from registered medical practitioners for the joint appointment of REGISTRAR in Obstetrics and Gynæcology. This post becomes vacant on 8th January, 1955. The appointment will be held for 1 year in the first instance, and be renewable for a further year. The successful candidate will be appointed to work for the first year mainly at Southmead Hospital, Bristol, including Obstetric Flying Squad duties. He may also be required to undertake duties at other hospitals in the Group.

Applications, stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 30th October, 1954.

CHELMSFORD HOSPITALS. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer) to large surgical units, for a period of 12 months.

Applications, stating age, sex, qualifications, and experience, with recent testimonials, should be sent to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Locum MEDICAL REGISTRAR required, 22nd November–3rd December.

Apply Group Secretary, Royal West Sussex Hospital, Chichester.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (276 Beds.) OBSTETRIC HOUSE SURGEON. The above post, which is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G., becomes vacant at the end of November, 1954. National Health Service salary and conditions.

Applications, together with 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (276 Beds.) GENERAL SURGICAL AND ORTHOPÆDIC HOUSE SURGEON. The above post, which is recognised for the F.R.C.S. Diploma, becomes vacant in mid-November. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (276 Beds.) PÆDIATRIC HOUSE PHYSICIAN. The above post, recognised for D.C.H., includes work in the ward and Outpatient Department and also provides experience in the care of the newborn. Opportunities exist for the study of preventive medicine among children and child guidance work. Post becomes vacant early December, 1954. National Health Service salary and conditions.

Applications, together with 2 testimonials, to be addressed to the Hospital Secretary at the above Hospital.

COLCHESTER. ESSEX COUNTY HOSPITAL. (188 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and Radiotherapy Departments. Post tenable for 6 months or 1 year. Recognised for F.R.C.S.

Applications, with copies of 3 testimonials, should be forwarded to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR (obstetrics and gynæcology). Resident post for duties at Mayday Hospital and St. Mary's Maternity Hospital. Unit is comprised of 113 obstetric and 47 gynæcological beds. Post vacant from 1st January, 1955.

Application forms obtainable from GEORGE A. PAINES, Secretary, Hospital Management Committee, General Hospital, Croydon, to be returned by 1st November.

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Radiology (diagnostic). Whole-time, non-resident, for Group. Candidates should have a Diploma in Radiology. Hospitals in Group may be visited by appointment with Radiologist.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, Croydon, to be returned immediately.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (neurosurgery) required. Duties also at other hospitals in the Derby group. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Resident SENIOR HOUSE OFFICER (Orthopædic and Accident Service), vacant immediately. Recognised for F.R.C.S.

Apply, with full details and copies of 2 recent testimonials, to Hospital Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (casualty), vacant immediately. Recognised for F.R.C.S.

Apply, with full details and copies of 2 recent testimonials, to Hospital Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Senior HOUSE OFFICER (ophthalmic), required immediately. Recognised for F.R.C.S.

Apply, with full details and copies of 2 recent testimonials, to Hospital Secretary.

DEWSBURY, YORKSHIRE. STAINCLIFFE GENERAL HOSPITAL. HOUSE OFFICER in General Surgery (first, second, or third post), vacant 1st November, tenable for 6 months. This post is a recognised pre-registration appointment. The Hospital has a Surgical Unit of 66 Beds and is recognised for the F.R.C.S.

Applications, with full details, quoting this journal, to be sent to the Administrative Officer at the Hospital.

DONCASTER HOSPITAL MANAGEMENT COMMITTEE. HAMILTON ANNEXE, WESTERN HOSPITAL. (Recognised under the Regulations for the D.Obst.R.C.O.G. and M.R.C.O.G. (obstetrical experience), and approved for Pre-registration Service under the Medical Act, 1950.) Applications are invited for the post of OBSTETRICAL HOUSE OFFICER (Senior House Officer or pre-registration post). Post vacant middle November.

Applications, stating age, nationality, qualifications and experience, and accompanied by copies of 2 testimonials, should be forwarded to the Secretary to the Committee at Doncaster Royal Infirmary.

FARNBOROUGH HOSPITAL, Farnborough, Kent. (800 Beds.) ORTHOPÆDIC SENIOR HOUSE OFFICER required immediately for 6 months. Deduction for residence £150.

Apply, stating age, qualifications with dates, experience, and naming 3 referees, to the Administrative Officer.

EDINBURGH. GOGARBURN INSTITUTION BOARD OF MANAGEMENT. JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female), for the above Hospital. Salary according to scale. Excellent opportunity for training in all branches of mental deficiency and child psychiatry.

Applications to Physician-Superintendent, Gogarburn Hospital, Corstorphine, Edinburgh, 12.

EDINBURGH. GOGARBURN INSTITUTION BOARD OF MANAGEMENT. HOUSE OFFICER. Applications are invited for the above post. The Institution is a recognised training school for the D.P.M., offers scope for wide experience in all branches of mental deficiency and child psychiatry, and is attached to Edinburgh University for teaching purposes. Accommodation available for unmarried person only.

Applications to the Physician-Superintendent, Gogarburn Hospital, Corstorphine, Edinburgh, 12.

EAST KILBRIDE. HAIRMYRES HOSPITAL. Applications are invited for the post of Full-time JUNIOR HOSPITAL MEDICAL OFFICER in the Thoracic Surgery Unit. Salary and conditions of service in accordance with national agreements.

Applications, stating age, and giving full details of education, experience and training, together with the names of 3 referees, should be submitted not later than 14 days from the date of publication of this advertisement to the Physician-Superintendent.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (715 Beds.) SENIOR SURGICAL CASUALTY HOUSE OFFICER (resident), required at above Hospital, vacant 25th October, 1954.

Apply immediately stating age, qualifications and details of experience, together with the names and addresses of 2 referees, to Group Secretary, Edgware General Hospital.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. 2 RESIDENT HOUSE SURGEONS for above Hospital. Posts vacant 15th and 17th November, 1954. 6 months appointments. Posts recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, experience, and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 23rd October, 1954.

EPPING. ST. MARGARET'S HOSPITAL. (485 Beds.) RESIDENT SENIOR HOUSE OFFICER (surgery) as Casualty Officer and Orthopædic House Surgeon. Vacancy approximately 3rd November, 1954. Recognised training post for F.R.C.S. Busy general hospital with easy access to London. Salary on national scale, less deduction for board, lodging, &c.

Applications, with copies of 2 testimonials, to the Group Secretary, Epping Group Hospital Management Committee, St. Margaret's Hospital, Epping, Essex, by 22nd October.

EPSOM, SURREY. WEST PARK HOSPITAL (for all stages of nervous and mental disorders). WEST PARK HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for 2 appointments of REGISTRAR in Psychiatry at above Hospital. Candidates may be of either sex. Single residential quarters are available.

Applications (5 copies) should be made on forms to be obtained from the Secretary to the Hospital Management Committee at the Hospital, to whom they should be returned not later than 29th October.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (117 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SURGICAL REGISTRAR required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

GRIMSBY GENERAL HOSPITAL. Grimsby Hospital MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER for casualty duties required immediately. Resident post. Recognised by Royal College of Surgeons for the Final Fellowship examination. Hours: Normally 9 A.M.–6 P.M. Monday–Friday; 9 A.M.–12 NOON Saturday, sharing night duty on rota with all other resident staff. Establishment consists of Senior Hospital Medical Officer (casualty) and the post now being advertised. The Hospital possesses a well-equipped medical library.

Applications, with the names and addresses of 2 referees, to the Hospital Secretary, Grimsby General Hospital.

GUILDFORD. ROYAL SURREY HOSPITAL. Guildford GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of MEDICAL REGISTRAR (resident) at above Hospital, which will be vacant on 1st January, 1955. Candidates may visit the Hospital by arrangement direct.

Application forms may be obtained from, and should be returned not later than 29th October, 1954, to, Secretary, Guildford Group Hospital Management Committee, St. Luke's Hospital, Guildford.

GUILDFORD. ST. LUKE'S HOSPITAL. South West METROPOLITAN REGIONAL HOSPITAL BOARD. GUILDFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SURGICAL REGISTRAR (resident) in the General Surgical Unit (60 Beds including children) at above Hospital. Preference will be given to candidates holding higher qualifications. The Hospital may be visited by arrangement with the Medical Superintendent.

Application forms from Group Secretary, Guildford Group Hospital Management Committee, at St. Luke's Hospital, Guildford (stamped, addressed envelope), to whom they should be returned within 14 days of the appearance of this advertisement.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL. HOUSE OFFICER (anæsthetics), non-resident.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent immediately to the Medical Superintendent.

GLASGOW ROYAL INFIRMARY. Senior House Officer in Surgery (Maxillo-facial Unit). Duties at above Infirmary.

Write, giving 3 names for reference, not later than 23rd October, 1954, to the Secretary, Board of Management for Glasgow Royal Infirmary and Associated Hospitals, 135, Buchanan-street, Glasgow, C.1.

GLASGOW ROYAL INFIRMARY. Senior House Officer in Anæsthetics. Duties at above Infirmary.

Write, giving 3 names for reference, not later than 23rd October, 1954, to the Secretary, Board of Management for Glasgow Royal Infirmary and Associated Hospitals, 135, Buchanan-street, Glasgow, C.1.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. Locum RESIDENT ANÆSTHETIST (Senior House Officer grade) required for 2 weeks from 10th November, 1954.

Applications to Medical Administrator.

HITCHIN HOSPITALS, Hitchin, Hertfordshire. Applications are invited for the post of RESIDENT HOUSE SURGEON at the North Herts Hospital, vacant 1st December, 1954. Recognised for F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital, Hitchin.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds. 3 Resident Medical Officers.) SENIOR HOUSE OFFICER (recognised for the F.R.C.S.). Post vacant now. Duties of Resident Surgical Officer. Appointment for 1 year.

Applications, giving particulars of qualifications, experience, &c., and naming 2 referees, to the Administrative Officer as soon as possible.

HUDDERSFIELD. ST. LUKE'S HOSPITAL. (262 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade) at the above Hospital to commence duties on 25th October, 1954. The Hospital at present caters for chronic sick, children and maternity patients but during the coming months the work will be extended by the opening of a theatre and acute block. Salary in accordance with the terms and conditions of service for hospital medical and dental staffs, £775–£50–£1075.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HULL. KINGSTON GENERAL HOSPITAL. (444 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE PHYSICIAN. There are 2 Junior House Physicians. Resident post. Salary £745, less £155 for emoluments. Vacant early November.

Applications, with full particulars, to the Hospital Secretary.

IPSWICH BOROUGH GENERAL HOSPITAL. (273 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (resident Anæsthetist), now vacant. The post, which is normally of 1 years duration, is recognised for the D.A. and the F.F.A.R.C.S. examinations.

Applications, stating age, nationality, together with recent testimonials, to Hospital Secretary.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. (1150 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Pathology (resident or non-resident), whole-time, vacant December. General laboratory and emergency duties, with training in all branches. Previous experience desirable. Candidates may visit Hospital by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 30th October, 1954.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (non-resident), vacant January. Possession of the D.A. desirable. Recognised for the F.F.A.R.C.S. The department comprises 3 teams and every kind of surgical work is carried out except thoracic and neurosurgery.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 30th October, 1954.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. (520 Beds.) SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Whole-time REGISTRAR in Anæsthetics to the Kingston Group of hospitals which becomes vacant on 11th November, 1954. The post is normally resident but consideration would be given to the use of a duty room. Possession of the D.A. will be an advantage.

Application forms should be obtained from the Group Secretary, 35, Coombe-road, Kingston-on-Thames, and returned to him not later than 2 weeks from the date of this insertion.

LEICESTER ROYAL INFIRMARY. (507 Beds.) Sheffield REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (ophthalmology) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEEDS. THE UNITED LEEDS HOSPITALS. Maternity HOSPITAL AT LEEDS. RESIDENT SURGICAL OFFICER of Registrar status required from 1st January, 1955, for 1 year in the first instance.

Applications, stating age, qualifications, previous posts with dates, with 3 names for reference, should be sent to the Sub-Dean, School of Medicine, Leeds, 1, before 30th October.

LEEDS. UNITED LEEDS HOSPITALS. The General INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER required for Professorial Department of Psychiatry attached to this teaching hospital, from mid-December. The post is non-resident and will be of 1 years duration.

Applications, giving age, qualifications, and previous posts with dates, with 3 names for reference, should be sent to the Secretary to the Board not later than 30th October.

LEEDS REGIONAL HOSPITAL BOARD AREA. Medical ACT, 1950. RESIDENT HOUSE OFFICER posts. Recognised pre-registration House posts will be available for the 6 months commencing 1st November, 1954, in the following hospitals approved under the Medical Act, 1950.

Scarborough Hospital (191 Beds)
1 Surgical (general surgery, orthopædic and E.N.T.).
1 Surgical (gynæcology and ophthalmology).
1 Medical.

County Hospital, York (222 Beds)
2 Surgical (general surgery and gynæcology). Recognised for F.R.C.S.

City Hospital, York (178 Beds)
1 Medical.

Hull Royal Infirmary and Sutton (242 Beds)
1 Surgical (ophthalmology). Recognised for D.O.M.S.
1 General Surgical (recognised for F.R.C.S.).
1 Surgical (orthopædic).

Kingston General Hospital, Hull (398 Beds)
1 Surgical (general surgery, gynæcology and orthopædic).

Westwood Hospital, Beverley (202 Beds)
1 Medical.

East Riding General, Driffield (249 Beds)
1 Medical.

Clayton Hospital, Wakefield (200 Beds)
1 Surgical (general surgery, E.N.T., and ophthalmology). Recognised for F.R.C.S.
1 Medical (general medical and pædiatric).

Pinderfields General, Wakefield (663 Beds)
1 General Surgical.
1 Medical.
1 Medical (neurology).
1 Surgical (thoracic).

General Hospital, Dewsbury (119 Beds)
1 Medical (general medical, pædiatric and dermatology).

Staincliffe General, Dewsbury (314 Beds)
1 Surgical (general surgery, orthopædic and E.N.T.).

Huddersfield Royal Infirmary (304 Beds)
1 General Surgical (recognised for F.R.C.S.).
1 Surgical (obstetrics and gynæcology). Recognised by R.C.O.G.

Royal Halifax Infirmary (301 Beds)
1 Surgical (ophthalmology and E.N.T.).
2 Medical.

Halifax General Hospital (425 Beds)
1 Medical.

Bradford Royal Infirmary (507 Beds)
1 Surgical (general surgery and urology). Recognised for F.R.C.S.
2 Surgical (orthopædic and casualty). Recognised for F.R.C.S.
1 Medical.

St. Luke's Hospital, Bradford (828 Beds)
1 Medical.
1 Medical (pædiatric).

Keighley Victoria Hospital (144 Beds)
1 Surgical (general surgery, orthopædic and E.N.T.). Recognised for F.R.C.S.

Otley General Hospital (170 Beds)
1 Medical (general medical and pædiatric).

St. James's Hospital, Leeds (1539 Beds)
3 General Surgical (recognised for F.R.C.S.).
1 Surgical (gynæcology). Recognised by R.C.O.G.
1 Surgical (plastic).
1 Surgical (urology).
7 Medical.
1 Medical (geriatric).
1 Medical (pædiatric).
1 Medical (dermatology).

St. Mary's Hospital, Leeds (216 Beds)
1 Midwifery (recognised by R.C.O.G.).

Seacroft Hospital, Leeds (60 pædiatric beds)
1 Medical (pædiatric).
1 General Surgical.

Harrogate and District General (249 Beds)
2 General Surgical (recognised for F.R.C.S.).

Candidates should express, where applicable, their preference for medical, surgical or midwifery posts within the same hospital on the application form.

Candidates wishing to apply for posts at more than 1 hospital should complete a separate form in respect of each hospital.

Application forms can be obtained from the Senior Administrative Medical Officer, Leeds Regional Hospital Board, Park-parade, Harrogate, or from the Dean, School of Medicine, Thoresby-place, Leeds, 2, and should be returned to either of the above named as soon as possible. Application may be made in advance of results of final examination.

LEEDS REGIONAL HOSPITAL BOARD invites applications for the following REGISTRAR posts :—

Ophthalmology

Duties at St. James's Hospital (22 eye beds) and the Public Dispensary, Leeds (non-resident).

Orthopædic Surgery

(a) Woodlands Orthopædic Hospital, Rawdon (100 Beds), and Orthopædic Outpatient Department, Bradford Royal Infirmary. Offers excellent training in all branches of accident and orthopædic surgery (may be non-resident).

(b) Royal Bath Hospital, Harrogate (40 orthopædic beds). Duties in connection with the Regional Rheumatism Scheme (resident).

(c) Duties mainly at Pinderfields General Hospital, Wakefield (70 short-stay and 160 long-stay orthopædic beds), and at other hospitals in the Wakefield A and B Groups (resident).

Otolaryngology

Duties at the Hull Royal Infirmary and associated hospitals (50 E.N.T. beds) (non-resident).

Applications, stating age, qualifications, and details of appointments held showing dates, with names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, not later than 21st October, 1954.

LEEDS, 2. PUBLIC DISPENSARY AND HOSPITAL. LEEDS A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of CASUALTY OFFICER (Senior House Officer) at the above Dispensary. The appointment will be for a period of 1 year. Salary in accordance with the agreed terms and conditions of service of hospital medical and dental staffs, with an appropriate deduction in respect of board, lodging, &c.

Applications, stating age, qualifications, experience, &c., together with the names of 2 referees, to be forwarded to the undersigned as soon as possible.

J. FOLKARD, Secretary to the Committee.

Administrative Offices, St. James's Hospital, Leeds, 9.

LINCOLN. COUNTY HOSPITAL. (200 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in Surgery and E.N.T., the post being recognised for D.L.O.

Apply giving full particulars to—

R. W. HOWICK, Group Secretary.

LIVERPOOL, 20. BOOTLE HOSPITAL. A vacancy exists for a RESIDENT CASUALTY OFFICER on the Junior Hospital Medical Officer grade.

Applications to the Secretary, Walton Hospital, Liverpool, 9.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for a post of PATHOLOGICAL REGISTRAR with duties at the Liverpool Stanley Hospital, Bootle Hospital and Waterloo Hospital for the period to 30th September, 1955. Reappointment for a further year will be considered without need for further application.

Apply by 27th October, 1954, on form obtainable from the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer), now vacant. The post offers varied experience and is recognised for the D.A. examination.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Secretary immediately.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in the Ophthalmic Department of the above Hospital. The Hospital is recognised by the Examining Boards for the F.R.C.S. and the D.O. Appointment will be for 12 months. Salary £745 a year, less £150 a year for residential emoluments. Post now vacant.

Applications should be forwarded as soon as possible to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Church-street, Maidstone.

MAIDSTONE. OAKWOOD HOSPITAL. Junior Hospital MEDICAL OFFICER required immediately for the above Mental Hospital of 2200 Beds. Salary scale £775 (for an officer appointed not less than 1 year after full registration as a medical practitioner)–£50–£1075 p.a. The appointment will be for 3 years in the first instance. Full residential accommodation is available for single officers. The appointment is subject to the National Health Service superannuation regulations and to conditions laid down by the Minister of Health.

Applications, in writing, giving the names of 2 persons to whom reference can be made, to be sent to the Medical Superintendent, Oakwood Hospital, Maidstone, Kent.

MARGATE. ROYAL SEA BATHING HOSPITAL. (241 Beds.) The post of SENIOR HOUSE OFFICER, now vacant, is primarily an orthopædic one, and affords experience in the treatment of tuberculous and non-tuberculous orthopædic conditions. There are also beds for the treatment of genito-urinary tuberculosis. The post is suitable for candidates for the Primary and the Final F.R.C.S. examinations. Salary £745 p.a., less £150 for residential emoluments.

Applications, with copies of testimonials, to the Hospital Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of NON-RESIDENT SENIOR REGISTRAR in E.N.T. Surgery in the South Manchester Group of hospitals, mainly at Wythenshawe Hospital, the Manchester Ear Hospital and the Manchester Hearing Aid Clinic. Arrangements may later be made for the person appointed to transfer to the United Manchester Hospitals to continue training.

Forms of application, obtainable from the Senior Administrative Medical Officer of the Board, Cheetwood-road, Manchester, 8, should be returned by 1st November, 1954.

MANCHESTER REGIONAL HOSPITAL BOARD. Birch HILL HOSPITAL. REGISTRAR in Obstetrics and Gynæcology. Post now vacant. Modern, busy unit. Recognised for D.Obst. R.C.O.G.

Apply at once to the Superintendent, Birch Hill Hospital, Rochdale, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Bury AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for REGISTRAR in Surgery at Bury General Hospital, the post falling vacant in October. Post recognised for F.R.C.S.

Applications, together with the names of 2 referees, should be sent to H. WILKINSON, Group Secretary.

Bury General Hospital, Bury, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in Psychiatry at Whittingham Hospital. House available for married man. If resident, comfortable furnished quarters are available with full residential emoluments at a charge of £140 p.a.

Applications, endorsed "Medical Officer," giving details of experience, and names and addresses of 3 referees, to be addressed to the Chairman, Whittingham Hospital, near Preston, and be received as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of RESIDENT REGISTRAR in the Board's Non-tuberculous Thoracic Surgery Unit of 58 Beds at Park Hospital, Davyhulme. 1 year appointment, renewable. Post vacant early December.

Application forms from Secretary, Park Hospital, Davyhulme, Urmston.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR (anæsthetics), resident, to the Burnley and District Group of hospitals. The hospitals are recognised for the purposes of the D.A.

Applications, together with the names and addresses of 3 referees, should be addressed to the Group Secretary, Burnley and District Hospital Management Committee, Burnley General Hospital.

MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT ANÆSTHETIST for joint duties at the Kent County Ophthalmic and Aural Hospital, and the West Kent General Hospital, Maidstone (total beds 254). The post, which will shortly be vacant, is of Senior House Officer grade, and carries a salary of £745 a year, with a deduction of £150 for residential emoluments. Excellent experience under Consultant Anæsthetists is available, and the post is recognised for the F.F.A.R.C.S. examination.

Applications, stating age, nationality, qualifications and experience, together with the names of 2 suitable referees, should be forwarded to the Administrative Officer, West Kent General Hospital, Maidstone.

MITCHAM. CUMBERLAND HOSPITAL, Whitford-gardens, MITCHAM, SURREY. (100 Beds.) SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. RESIDENT REGISTRAR in Tuberculosis. Applications are invited for the post of Resident Medical Officer (Registrar) at the above Hospital. Duties also in Thoracic Unit, St. Helier Hospital. Experience in specialty essential.

Form of application, returnable by 29th October, obtainable from the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

MOTHERWELL, HAMILTON AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. COUNTY HOSPITAL, STONEHOUSE. (500 Beds.) Immediate vacancies exist for 4 HOUSE OFFICERS (surgery).

(1) 2 in Orthopædic and Tuberculosis Unit.
(2) 1 in General Surgery.
(3) 1 in Gynæcology, E.N.T., &c.

These appointments are approved as pre-registration posts.

Applications to Medical Superintendent, County Hospital, Stonehouse, Lanarkshire.

MOTHERWELL, HAMILTON AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. COUNTY HOSPITAL, STONEHOUSE. (500 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical).

Applications to Medical Superintendent, County Hospital, Stonehouse, Lanarkshire.

MOTHERWELL, HAMILTON AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. COUNTY HOSPITAL, STONEHOUSE. (500 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (orthopædics). Applications are invited for the above resident post in the Orthopædic and Surgical Tuberculosis Department, commencing now. 250 Beds mainly surgical tuberculosis, but includes all casualty work. Salary scale £775–£50–£1075, less residential emoluments.

Applications to Medical Superintendent, County Hospital, Stonehouse, Lanarkshire.

NEWCASTLE GENERAL HOSPITAL. (861 Beds.) NEWCASTLE UPON TYNE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for a whole-time SENIOR HOUSE OFFICER (pædiatrics), resident, to the Children's Department in the above Hospital, to commence duties in December. Salary is in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). The department is actively associated with the Department of Child Health of Durham University, and the post offers good opportunities for gaining experience in many aspects of pædiatrics. The appointment is for 1 year in the first instance.

Applications, together with 1 copy of 2 testimonials, to be sent to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4, not later than 6th November, 1954.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the non-resident appointment of REGISTRAR in the Orthopædic Department at the Royal Victoria Infirmary. The successful candidate will be required to teach in his subject and preference will be given to applicants who have passed the Primary Fellowship examination.

Applications, giving full particulars and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Queen Victoria-road, Newcastle upon Tyne.

NEWPORT, MONMOUTHSHIRE. ROYAL GWENT HOSPITAL. (260 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER (E.N.T. and ophthalmic) required about 1st November. National salary, less £125 board-residence. Grade depends on period since qualification. Recognised D.L.O. Covers 23 E.N.T. and 8 eye beds.

Write, quoting 2 referees, to T. A. JONES, Group Secretary. 64, Cardiff-road, Newport, Mon.

NOTTINGHAM GENERAL HOSPITAL. Locum Third CASUALTY OFFICER required (Senior House Officer grade). Salary (less £150 emoluments) and conditions of service in accordance with Ministry regulations.

Applications, giving full details, to be sent to—

General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered general practitioners for the post of THIRD CASUALTY OFFICER (Senior House Officer grade). Salary (less £150 emoluments) and conditions of service in accordance with those laid down by the Ministry. Duties to commence as soon as possible. This post offers wide experience of casualty work. The Staff establishment requires only 1 night in 3 emergency work, and off duty permits time for study for higher examinations.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

General Hospital, Nottingham. HENRY M. STANLEY.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR ORTHOPÆDIC AND FRACTURE HOUSE OFFICER (locum tenens considered). The post offers exceptional experience in traumatic surgery. Duties to commence at the end of November. Salary and conditions of service in accordance with Ministry regulations. If resident £150 deducted for emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials to be sent to—

HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners (Male or Female—locum tenens considered) for the post of RESIDENT SENIOR ANÆSTHETIC HOUSE OFFICER. Duties to commence as soon as possible. Terms and conditions of service in accordance with published regulations of the Ministry of Health. £150 deducted for residential emoluments.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to—

HENRY M. STANLEY, Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of CLINICAL PATHOLOGIST (Senior House Officer grade), resident or non-resident, vacant 1st December. Previous experience in pathology not essential. Opportunities for training in all branches of clinical pathology are afforded in a department serving over 1200 beds. Salary and conditions of service in accordance with Ministry regulations.

Applications, with names and addresses of 3 referees, should be received before 30th October, addressed to the Secretary.

NOTTINGHAM AND MIDLAND EYE INFIRMARY. Required, SENIOR HOUSE OFFICER and HOUSE SURGEON for the above Hospital. Duties to commence on or about 20th October, 1954. Salaries and conditions of service in accordance with Ministry regulations.

Applications, stating age, qualifications and experience, together with testimonials, to be sent as soon as possible to—

HENRY M. STANLEY, Group Secretary.

General Hospital, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (804 Beds. Recognised for training for the D.A. and F.F.A.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, 1954, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

ORPINGTON HOSPITAL, Orpington, Kent. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Male) at Senior House Officer grade for above General Hospital (813 Beds). Post recognised for F.R.C.S.

Applications to the Physician-Superintendent.

OXFORD REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR in Obstetrics and Gynæcology, to the Hospitals of Reading and District Hospital Management Committee. Applicants should hold the M.R.C.O.G.

Applications on forms obtainable from the Secretary, Registrar Committee (from whom further details may be obtained), 43, Banbury-road, Oxford, should reach him by 5th November.

OXFORD. UNITED OXFORD HOSPITALS. Applications invited for post of NON-RESIDENT REGISTRAR in Pathology at the Radcliffe Infirmary, with effect from early November.

Applications on forms obtainable from Administrator, Radcliffe Infirmary, Oxford, to be returned not later than 30th October, 1954.

PERTHSHIRE MENTAL HOSPITALS. House Physicians (recognised pre-registration posts), at the Murray Royal Hospital, Perth (260 Beds), and The Hospital, Murthly, Perthshire (460 Beds).

Applications, with names of 2 referees, to the Group Physician-Superintendent, Murray Royal, who will on request answer inquiries or arrange for a visit to the Hospital.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment, vacant now, of REGISTRAR in the Chest Services of the Group for duties at the Portsmouth Chest Clinic and the tuberculosis wards at the Infectious Diseases Hospital and Saint Mary's Hospital, Portsmouth, including experience with a major Thoracic Surgery Unit.

Forms of application may be obtained from the Group Secretary, Portsmouth Group Hospital Management Committee, 35, Grove-road South, Southsea, which should be returned to him duly completed on or before 29th October, 1954. Canvassing will disqualify. Candidates may visit the above Clinic and Hospitals by arrangement with the Group Secretary.

POOLE GENERAL HOSPITAL, Longfleet-road, Poole, DORSET. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (anæsthetics). The Hospital is recognised for the D.A., and the F.F.A.R.C.S.

Applications to the Hospital Secretary.

POOLE GENERAL HOSPITAL, Longfleet-road, Poole, DORSET. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. 2 HOUSE SURGEONS (pre-registration) required. 1 post vacant 3rd December, 1954, and the other on 4th January, 1955. The Hospital is recognised for the F.R.C.S. and the F.R.C.S.E.

Applications to the Hospital.

PLYMOUTH CLINICAL AREA. The Board of Governors OF THE UNITED BRISTOL HOSPITALS AND THE SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited by the above Boards from registered medical practitioners for the joint appointment of SENIOR REGISTRAR in General Medicine. The appointment will be held for 1 year in the first instance but may be renewed thereafter on an annual basis. The successful candidate will be appointed to work for the first year mainly at the Plymouth, South Devon and East Cornwall Hospital, Plymouth, and to visit other hospitals in the Clinical Area as may be determined by the Regional Board from time to time.

Applications, stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 30th October, 1954.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Greenbank-road. Applications invited from registered dental practitioners for the appointment of RESIDENT DENTAL HOUSE SURGEON, vacant immediately. This appointment is recognised by the Royal College of Surgeons as fulfilling the requirements of candidates for the Fellowship of Dental Surgery.

Applications, stating age, nationality, and experience, together with copies of 3 recent testimonials, should be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PRESTON (near), LANCASHIRE. WHITTINGHAM HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (temporary, for a period of 6 months). Comfortable furnished quarters are available with full residential emoluments at a charge of £140 p.a.

Applications, endorsed "Medical Officer," giving details of experience and names and addresses of 3 referees, to be addressed to the Chairman, Whittingham Hospital, near Preston, and be received as soon as possible.

READING AREA HOSPITALS. Applications are invited for post of SENIOR HOUSE OFFICER or JUNIOR HOUSE OFFICER (pathology). Previous experience in pathology desirable but not essential. Salary £745 or £525 p.a. respectively, less £125 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, together with copies of recent testimonials, to Group Secretary, 3, Craven-road, Reading.

READING. ROYAL BERKSHIRE HOSPITAL. (403 Beds.) Applications are invited from registered medical practitioners for the appointment of JUNIOR HOUSE SURGEON (gynæcology), vacant 1st November. Post M.R.C.O.G. recognised and tenable for 6 months. £525 p.a., less £125 for board-residence.

Write, stating age, qualifications with dates, nationality, and present post, with copy of a recent testimonial, to the Secretary.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY. SENIOR HOUSE OFFICER (mainly surgical) required at above Hospital.

Apply to the Hospital Secretary.

ROCHDALE. BIRCH HILL HOSPITAL. Rochdale AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required at above Hospital. Pre-registration students eligible. Post recognised for 6 of the 12 months F.R.C.S. experience.

Apply to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancashire, at once with full details.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

SENIOR REGISTRAR in Bacteriology based at the Victoria Infirmary, Glasgow, with duties in Ayrshire and elsewhere within the Region as may be required.

SENIOR REGISTRAR in Pathology based at the Royal Infirmary, Glasgow, with duties in the Lanarkshire Area.

SENIOR REGISTRAR in Ophthalmology based at the Glasgow Eye Infirmary.

REGISTRAR in Radiodiagnosis at the Royal Infirmary, Glasgow.

REGISTRAR in Surgery at the Victoria Infirmary, Glasgow. These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, by 6th November, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (anæsthetics) required at the City General Hospital, Sheffield. This is a large general hospital with a Department of Thoracic Surgery, a Regional Cardiological Centre, and a Professorial Gynæcological Unit. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 25th October, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time Locum SURGICAL REGISTRAR required immediately at the Grantham and Kesteven General Hospital. Remuneration £16 per week.

Apply to the Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, naming 2 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SENIOR MEDICAL REGISTRAR for the Leicester Royal Infirmary. Appointment for 1 year in the first instance, reviewable annually. It has been agreed between the Sheffield Regional Hospital Board and the Board of Governors of the United Sheffield Hospitals that, subject to satisfactory work and progress, the tenure of the appointment will be divided between the Leicester Royal Infirmary and 1 of the Teaching Hospitals.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with the names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10, to arrive not later than 25th October, 1954.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRAR in Psychiatry required for Middlewood Hospital, Sheffield (2089 Beds). D.P.M. essential. House available. Appointment for 1 year in the first instance, reviewable annually. Opportunity for research and experience in the special branches of psychiatry available in the Hospital area.

Application forms and further details obtainable from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 1st November, 1954.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications are invited for the following posts :—

(*a*) NON-RESIDENT SENIOR REGISTRAR in Anæsthetics. The appointment is for 1 year in the first instance and will be reviewed annually. It has been agreed in principle between the Board of Governors of The United Sheffield Hospitals and the Sheffield Regional Hospital Board that the appointment, if extended to the full period of 4 years, will be divided, subject to satisfactory work and progress, between the United Sheffield Hospitals and a hospital in the Region.

Closing date for applications 30th October, 1954.

(*b*) NON-RESIDENT SURGICAL REGISTRAR at the Royal Hospital Unit.

Closing date for applications 23rd October, 1954.

(*c*) REGISTRAR to the Department of Dermatology at the Royal Infirmary Unit. Post vacant. A higher qualification preferable.

(*d*) RESIDENT REGISTRAR in Thoracic Surgery at the Royal Infirmary Unit. Post vacant 15th December. Previous experience in thoracic surgery essential.

Closing date for applications 30th October, 1954.

Applications for the above posts should state age, qualifications and experience, give the names of 3 referees, and be sent immediately (unless otherwise stated) to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as a Whole-time REGISTRAR in Psychiatry to fill a vacancy in the approved trainee establishment at Oakwood Hospital, Maidstone, Kent. Previous experience in general medicine is desirable. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th October, 1954.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Orthopædic Surgery to fill a vacancy in the approved trainee establishment at the Brighton and Lewes Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 30th October, 1954.

SOUTHEND-ON-SEA GENERAL HOSPITAL. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN (House Officer grade). Post vacant 17th December, 1954. Appointment primarily to Pædiatric Department, with duties in Cardiological and Skin Departments. Post recognised for D.C.H.

Applications, stating age, qualifications, and previous experience, with copies of recent testimonials, should reach the undersigned at the Hospital by 27th October, 1954.

J. C. FIELD, *Secretary.*

SOUTHEND-ON-SEA GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (surgical). Post vacant 1st December, 1954. Recognised for F.R.C.S.

Applications, stating age, qualifications, and experience, with copies of recent testimonials, should reach the undersigned at the Hospital by 27th October, 1954.

J. C. FIELD, Secretary.

SOUTHEND GENERAL HOSPITAL. (251 Beds.) Applications are invited from registered practitioners or from pre-registration candidates for the post of RESIDENT GENERAL HOUSE PHYSICIAN (House Officer grade), vacant on 23rd November, 1954.

Applications, &c., to reach the undersigned by 27th October, 1954. J. C. FIELD, Secretary.

SOUTHAMPTON EYE HOSPITAL. (32 Beds. Recognised for the D.O.M.S.) RESIDENT SENIOR HOUSE OFFICER required immediately. Salary £745 p.a.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON (near). COLDEAST HOSPITAL, SARISBURY GREEN, near SOUTHAMPTON. (783 mental deficiency beds.) JUNIOR HOSPITAL MEDICAL OFFICER required. Appointment tenable for any period up to 3 years. Salary £775, rising by 6 increments of £50 to £1075 p.a. Facilities will be given if required for attendance at the recognised neurological clinics and at Inpatient and Outpatient adult and children's Departments of nearby psychiatric hospitals for the purpose of qualifying for the D.P.M. or other diplomas. A 4-roomed bungalow is available if necessary for married candidates.

Applications should be sent to the Medical Superintendent, Coldeast Hospital, Sarisbury Green, near Southampton, from whom further particulars can also be obtained.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON to the Orthopædic Department. This appointment, which is for 6 months, is open to pre-registration candidates and is vacant at present.

Applications, stating age, nationality, and naming 2 referees, should be submitted to the Group Secretary, Odstock Hospital, Salisbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. (241 Beds.) SHREWSBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON in General Surgery. Post recognised for F.R.C.S. and approved for Pre-registration Service. Vacant 13th November, 1954.

Applications and copy testimonials to Group Secretary, Royal Salop Infirmary, Shrewsbury.

STAFFORD. STAFFORDSHIRE GENERAL INFIRMARY. (175 Beds.) RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer) required (Male or Female).

Applications, giving particulars of age, previous experience, and copies of 2 recent testimonials, to the Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (general surgery) required, vacant shortly. Hospital recognised for F.R.C.S. examination, and the post is recognised for experience during the pre-registration period.

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for RESIDENT ASSISTANT CLINICAL PATHOLOGIST to the Stoke-on-Trent Group of hospitals, vacant now. Single accommodation available at the North Staffs Royal Infirmary. The post is of Junior Hospital Medical Officer status, but applications from practitioners with less than the required 2 years qualification period will be considered, in the grade of Senior House Officer. The post offers exceptional experience in hospital laboratory work and the laboratory is recognised for the Diploma in Clinical Pathology and also for the Diploma in Pathology.

Applications, stating age, nationality, and full details of previous appointments held, together with copies of 3 recent testimonials, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE *ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT* COMMITTEE. Applications invited for SENIOR HOUSE OFFICER (orthopædics). Post recognised for F.R.C.S.

Apply, stating age and nationality, together with details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (general surgery) required. Hospital recognised for F.R.C.S. examination, and post recognised for experience during the pre-registration period.

Apply, with copy testimonials, stating age, nationality and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

SULLY HOSPITAL, Sully, Penarth, Glamorgan. (Thoracic Centre—324 Beds.) CARDIFF HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (medical) required immediately. Experience gained in treatment of chest diseases in adults and children.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (382 Beds.) CASUALTY OFFICER (Registrar grade) required for the above Hospital. Post recognised for the F.R.C.S. regulations. Appointment tenable for 6 months, subject to review at the end of this period.

Application forms obtainable from, and returnable to, Group Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catharine-street, St. Albans, by 1st November, 1954.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (382 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR required. Post vacant 11th January, 1955. Preference given to candidates having considerable experience in dealing with medical emergencies. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, by 1st November, 1954.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. HOUSE SURGEON required (pre-registration post).

Applications, stating age and qualifications, to Hospital Secretary before 1st November.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of ANÆSTHETIST (Senior House Officer grade) at Swansea Hospital. The Hospital is recognised under D.A. regulations.

Applications, stating age, qualifications and experience, should be addressed to the Group Secretary, Glantawe Hospital Management Committee, St. Helen's-road, Swansea.

SWANSEA. MOUNT PLEASANT HOSPITAL. Glantawe *HOSPITAL MANAGEMENT COMMITTEE. Registered medical practitioners* are invited to apply for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (Female) for work in the Medical and Surgical Departments, and in the chronic sick wards of the above Hospital.

Applications, stating age, experience and qualifications, should be addressed to the Group Secretary, Glantawe Hospital Management Committee, St. Helen's-road, Swansea.

TAUNTON. TONE VALE GROUP HOSPITAL MANAGEMENT COMMITTEE, NORTON FITZWARREN, TAUNTON, SOMERSET. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER, with duties mainly at Tone Vale Hospital, a modern Psychiatric Hospital of 1085 Beds treating all forms of mental and nervous disorder and including a new unit for psychotic children. The post provides an excellent opportunity for postgraduate training in psychiatry, including outpatient clinic work, and every facility is provided for study for the D.P.M. Accommodation at a moderate charge is available for a single or married officer. The appointment, tenure of which will in the first instance be limited to 3 years, is subject to the terms and conditions of service for hospital medical staff, the salary scale being £775–£1075 p.a.

Applications, including details of age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Group Secretary, within 10 days of the appearance of this advertisement.

TORQUAY. TORBAY HOSPITAL. Resident Casualty OFFICER (Senior House Officer status) required for 1st November, 1954.

Applications, stating qualifications, nationality, age, with copies of testimonials (quoting ref. F955/48), to the Group Secretary, Torquay District Hospital Management Committee, 62/64, East-street, Newton Abbot, S. Devon.

WARRINGTON INFIRMARY. Applications are invited from qualified practitioners for the vacancy of RESIDENT ANÆSTHETIST (Senior House Officer grade), Male or Female, at the Warrington Infirmary. The Infirmary is recognised for the D.A. examination. Scale of salary £745 p.a., less £130 p.a. for residential emoluments.

Applications to—

H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee,
c/o General Hospital, Warrington, Lancs.

WARWICK (near). CENTRAL MENTAL HOSPITAL. SENIOR HOUSE OFFICER required on 1st November in this Mental Hospital of 1400 Beds with Neurosis Unit, 4 adult and 2 child psychiatry clinics recognised for the D.P.M. and Departments of Electro-encephalography, Occupational Therapy, Psychology and social work. A modern house is available.

Applications, together with the names and addresses of 3 referees, to the Medical Superintendent within 14 days of the appearance of this advertisement.

WATFORD AND DISTRICT PEACE MEMORIAL HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. RADIOLOGICAL REGISTRAR required for the above Hospital. Hospital may be visited by direct appointment.

Application form obtainable from, and returnable to, the Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

WATFORD. SHRODELLS HOSPITAL. (General Hospital—420 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric Unit. Adequate time is available for reading.

Applications, together with copies of not more than 2 recent testimonials, should reach the Medical Officer-in-charge as soon as possible.

WELSH REGIONAL HOSPITAL BOARD.

SURGICAL REGISTRAR (plastic surgery), St. Lawrence Hospital, Chepstow. Expected to visit other hospitals in South Wales area. Considerable opportunities for training in specialty. Accommodation for single person. Subject to review at end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WEST BROMWICH AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE GROUP NO. 18. THE MIDLAND CENTRE FOR NEUROSURGERY, SMETHWICK HOSPITAL, Holly-lane, SMETHWICK. RESIDENT SENIOR HOUSE OFFICER required for this Hospital devoted to the care of neurosurgical and neurological patients. This Hospital is just opening, and this resident appointment will be for work in both surgical and medical wards. This appointment is well suited for those studying for higher medical or surgical examinations.

Applications, together with 3 testimonials, should be submitted to Mr. J. O. ROBINS, Group Secretary, at the West Bromwich and District General Hospital, Edward-street, West Bromwich.

WINDSOR. KING EDWARD VII HOSPITAL. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON required, Male or Female, for post vacant 1st December. Obstetric post recognised for D.Obst.R.C.O.G. Successful candidate will be resident at Old Windsor Unit of Hospital. Applicants required to be members of Medical Protection Society.

Applications, stating age, nationality, qualifications with dates, with copies of recent testimonials or names of 3 referees, to Hospital Secretary by 30th October.

WINDSOR. KING EDWARD VII HOSPITAL. Casualty OFFICER required (Senior House Officer grade). Department forms part of Accident Service of the Windsor Group; duties include House Surgeon to E.N.T. and Eye Departments. Previous experience in treatment of acute injuries desirable.

Applications, stating age, qualifications with dates, and nationality, with copies of recent testimonials, to Hospital Secretary.

WIGAN AND LEIGH HOSPITAL MANAGEMENT *COMMITTEE. SENIOR HOUSE OFFICER in General Surgery* required for duty at Billinge Hospital, Orrell, near Wigan (370 Beds). Post vacant.

Applications, with names of 2 referees, to Secretary, Knowsley House, Wigan.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER (anæsthetics), resident, for duties at the above and other hospitals in the Group. Post recognised for F.F.A.R.C.S. examinations. Facilities for experience in major thoracic and orthopædic work.

Applications to Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery required. Post now vacant.

Applications to Secretary, Wigan Infirmary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (311 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 7th December.

Applications, with copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON GROUP.

The Royal Hospital, Wolverhampton (An Associated Hospital of the University of Birmingham Medical School) SENIOR HOUSE OFFICER (anæsthetist). Appointment recognised for D.A. and F.F.A.R.C.S. Vacant 15th November.

Wolverhampton and Midland Counties Eye Infirmary (Recognised for F.R.C.S. and D.O. examinations)
SENIOR HOUSE OFFICER, vacant 7th November.

Applications, with copies of 3 recent testimonials, to be sent to Group Secretary, The Royal Hospital, Wolverhampton.

WORCESTER (near). POWICK HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (resident or non-resident). The post offers experience in all branches of psychiatry, including all forms of modern treatment and outpatient clinics. The Hospital has a high admission-rate, is recognised for the D.P.M., and has associated Child Guidance Clinics and a Mental Deficiency Institute similarly recognised. Arrangements are made for Medical Officers to attend at the Birmingham Medical School for instruction in neurology.

Applications, with full details and the names of 2 referees, to be forwarded to the Medical Superintendent.

YORK A AND TADCASTER HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required immediately for E.N.T. Department (30 Beds). Post recognised for D.L.O.

Applications, giving age, nationality, qualifications, experience, and names of 2 referees, to Secretary, Bootham Park, York.

YORKSHIRE. EAST RIDING HOSPITAL MANAGEMENT COMMITTEE.

Westwood Hospital, Beverley, Yorks (229 Beds)

(*a*) ASSISTANT PATHOLOGIST (Senior House Officer) required in Area Laboratory, with attendance Branch Laboratory at Driffield. Offers experience all branches pathology.

Northfield Sanatorium, Driffield, Yorks (78 Beds)

(*b*) SENIOR HOUSE PHYSICIAN, vacant now. Offers experience all branches tuberculosis within Group, including surgery, M.M.R. and clinics. Time for study. Ex-patients welcome.

Broadgate (Mental) Hospital, Beverley, Yorks (650 Beds)

(*c*) JUNIOR HOSPITAL MEDICAL OFFICERS (2), required now.

Salary for (*a*) and (*b*) £745 and for (*c*) £775–£50–£1075.

Detailed applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

NORTHERN IRELAND TUBERCULOSIS AUTHORITY. Applications are invited for the post of ASSISTANT MEDICAL OFFICER to undertake B.C.G. vaccination work in No. 4 Area which is comprised of County Londonderry and the northern part of County Antrim. Applicants should have held house appointments and have not less than 2 years experience after registration. The person appointed, who will have his Headquarters at Londonderry, will act under the general control and supervision of the Physician in charge of the B.C.G. Service. The remuneration for the post will be £775–£50–£1075 p.a.

Forms of application and conditions of appointment may be obtained from the Secretary, Northern Ireland Tuberculosis Authority, 27, Adelaide-street, Belfast, with whom completed applications should be lodged not later than 20th October, 1954.

B.W.I. GENERAL HOSPITAL, Barbados. Applications are invited for appointment as HOUSE OFFICER (pre-registration appointment) at the above Hospital for 1 year (for surgical and medical duties, each of 6 months duration). Appointment will be on agreement. Candidates should apply at least 6 months before the date of their final examination and should confirm from their Licensing Bodies that the post is acceptable to them for pre-registration training for the purpose of the Medical Act, 1950. Salary $1680 (£350) a year. Income-tax at local rates. Quarters not provided. Passage to Barbados, 1 single fare not to exceed $523.20 (£108). 2 weeks vacation at end of each 6-monthly period.

Applications should be made to Director of Medical Service, Barbados, quoting reference 1740/1939.

NEW YORK. ALBANY HOSPITAL, Albany, New York, U.S.A. NEUROLOGY RESIDENCIES available in 700-Bed, university-teaching, general hospital. Salary range $1620–$2220 annually, plus laundry, uniforms and room.

Address inquiries to Medical Director.

NEW YORK. ALBANY HOSPITAL, Albany, New York, U.S.A. PSYCHIATRY RESIDENCIES available in 700-Bed, university-teaching, general hospital, with 60-Bed acute treatment Psychiatric Unit fully approved for 3 years training. Experience includes dynamically-oriented psychotherapy with children and adults, shock therapies and neurologic training. Salary range $1620–$4000 annually plus laundry, uniforms and room.

Address inquiries to Medical Director.

NEW YORK. ALBANY HOSPITAL, Albany, New York, U.S.A. INTERNSHIPS and RESIDENCIES available in 700-Bed general, private Albany Hospital, directly connected with Albany Medical College. Approved for all major specialties. Participating in exchange-visitor programme. Salary range $1320–$2220 annually in addition to laundry, uniforms and room. All appointments begin 1st July, 1955.

For further information apply to Medical Director.

NEW YORK. NEW ROCHELLE HOSPITAL, New ROCHELLE, NEW YORK, U.S.A. (360-Bed general community hospital.) Approved by the Joint Commission on Accreditation of Hospitals. Also approved by the American College of Surgeons and American Medical Association for internship and residency training. Only graduates from approved university schools accepted. 2 INTERNSHIPS available for the term commencing 1st January, 1955. Stipend is $200 per month, plus complete maintenance. Passage back to England paid by Hospital after completion of 12-month internship.

Apply Superintendent.

Public Appointments

BLACKPOOL. COUNTY BOROUGH OF BLACKPOOL. SCHOOL MEDICAL SERVICE. Applications are invited for the appointment of FIRST ASSISTANT SCHOOL MEDICAL OFFICER from registered medical practitioners (Male or Female). Preference will be given to applicants with experience in the examination and treatment of children and in the assessment of educationally retarded children. The possession of the D.P.H. and/or D.C.H., with experience in refraction work, will be an advantage. The salary payable in respect of the appointment will be £1100 p.a., rising by annual increments of £50 to a maximum of £1400 p.a. and experience and qualifications will be taken into account when fixing the commencing salary. The appointment will be subject to the provisions of the National Health Service (Superannuation) Regulations, 1947 and 1948, and the person appointed will be required to contribute to the superannuation fund maintained by the Council.

Forms of application and conditions of appointment may be obtained from the Medical Officer of Health and Principal School Medical Officer, Municipal Health Centre, Whitegate-drive, Blackpool, and should be returned to reach him not later than Saturday, 30th October, 1954.

TREVOR T. JONES, Town Clerk.

AMENDED ADVERTISEMENT

BUCKINGHAMSHIRE, COUNTY OF BUCKS. Borough OF SLOUGH. Applications are invited from registered medical practitioners holding the qualifications prescribed by the Sanitary Officers (Outside London) Regulations, 1935 and 1951, for the whole-time joint appointment of ASSISTANT COUNTY MEDICAL OFFICER AND DEPUTY MEDICAL OFFICER OF HEALTH for the Borough of Slough. Salary within the scale of £979 3s. 4d.–£1323 9s. 8d. p.a. Travelling and subsistence allowances will be paid on the County Council's scale. The appointment is superannuable, and subject to medical examination.

Further particulars and forms of application may be obtained from the undersigned, to whom applications must be delivered by 30th October, 1954. *Note:* Closing date 30th October—not 30th November as previous advertisement.

GUY R. CROUCH, Clerk of the Bucks County Council.
NORMAN T. BERRY, Town Clerk, Slough.

CITY OF WESTMINSTER. Applications are invited from medical practitioners to act as the Council's MEDICAL EXAMINER from 25th March next. Duties comprise mainly examination as and when necessary of members and prospective members of Council's staff and submission of written reports. Remuneration will be :—

(i) 25s. per case where the examinee attends the Medical Examiner or is visited by him within a 2-mile radius.
(ii) 35s. per case where the Medical Examiner visits the examinee outside such 2-mile radius.

The average cases and fees paid in the last 3 years were 183 and £229 respectively. Candidates must have consulting-room within the City of Westminster.

Applications, accompanied by the names and addresses of 2 referees, and giving full particulars of age, qualifications and experience, together with the address of consulting-room, to the Town Clerk, Westminster City Hall, Charing Cross-road, W.C.2, by 15th November, 1954.

COVENTRY. CITY OF COVENTRY. Applications are invited for joint post of SCHOOL MEDICAL OFFICER AND ASSISTANT MEDICAL OFFICER OF HEALTH for duties connected with medical inspection and clinic treatment of school-children, also maternity and child welfare work and such other duties as the Medical Officer of Health and Principal School Medical Officer may include from time to time. Qualifications and experience in ascertainment of handicapped pupils an advantage. Salary £950–£1300. Commencing salary according to previous experience/qualifications.

Applications and further particulars to Principal School Medical Officer, Council House, Coventry.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 8, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
ASTON	WARWICK	30TH OCTOBER, 1954
HOWDEN	YORK	30TH OCTOBER, 1954
TROON	AYR	30TH OCTOBER, 1954
MARGATE	KENT	30TH OCTOBER, 1954
ABERSYCHAN ..	MONMOUTH ..	30TH OCTOBER, 1954

HER MAJESTY'S COLONIAL SERVICE. (Medical BRANCH.) ADEN. MEDICAL OFFICERS are required for general duties in the Medical Department of Aden. Candidates should have had some experience either of anæsthetics and preferably possess the F.F.A.R.C.S. or the D.A. (if obtained prior to November, 1953) or of venereal and skin diseases. Appointment can be made on a permanent basis with pension at age of 45–55, or on short-term contract with gratuity on satisfactory completion of service. Candidates in the National Health Service may resign from the National Health Service but retain their superannuation rights (up to 6 years) and receive a gratuity of 20% of the aggregate of their salary at the end of their engagements. Salary scale (including expatriation pay) ranges from £1212 to £1999 a year or, if in possession of the F.F.A.R.C.S. or D.A. (prior to November, 1953) £1404 to £1999 a year. Starting salary is determined according to the candidate's qualifications and experience. Pension in the case of permanent appointment is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. The gratuity in respect of contract appointments, is at the rate of £37 10s. for each completed 3 months of service, payable on satisfactory completion of contract. An outfit allowance of £30 is payable on appointment. Furnished quarters are provided at low rental. Income-tax at local rates. Free passages are provided for Officer and wife, and up to 4 children under the age of 18. Tour of service is from 18 to 24 months. Local leave is permissible and generous home leave is granted after each tour. Candidates must possess medical qualifications registrable in the United Kingdom.

Application forms can be obtained from the Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. CDE.117/2/01).

HER MAJESTY'S OVERSEA CIVIL SERVICE. (Medical BRANCH.) UGANDA. MEDICAL OFFICERS required for general medical duties and to assist with the training of sub-ordinate African medical staff. Appointment can be made (subject to 2 years probation) on a permanent basis with pension (non-contributory) at the age of 45–55, or on short-term contract with gratuity. Candidates in the National Health Service may resign from the National Health Service but retain their super-annuation rights (up to 6 years) and receive a gratuity of 20% of the aggregate of their salary at the end of their engagements. Salary scale ranges from £865 to £1590 p.a., plus a temporary (non-pensionable) cost-of-living allowance of 35% of salary, subject to a maximum of £350 p.a. Starting-point in the scale is determined according to age, qualifications and experience. Pension is earned at the rate of 1/600th of the final pensionable emoluments for each completed month of service. The gratuity in respect of contract appointments is payable on satisfactory completion of contract service at the rate of £100–£150 p.a. Quarters are provided with heavy furniture, at a rental of 10% of salary (7½% of salary if unfurnished). Free passages in both directions are provided for Officer and wife, and up to cost of 1 adult fare for children. Income-tax at local rates. Local leave is permissible and generous home leave is granted after each tour of from 30–36 months duration. Educational facilities are available in East Africa. Consulting practice in certain circumstances is allowed outside Government Institutions. Candidates must possess qualifications registrable in the United Kingdom.

Application forms can be obtained from the Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith-street, London, S.W.1 (quoting reference No. BCD.117/9/02).

KUWAIT. GOVERNMENT OF KUWAIT. Department OF HEALTH. Applications are invited for the following posts :—

(1) SURGEON for the State Hospital. Must have the F.R.C.S. England, or show evidence of having attained a similar academic level. An experience of accident and fracture work is essential, as besides general surgery the appointee will be expected to organise and carry out all the surgery of trauma. Salary £3250–£150–£3700 p.a., plus car allowance. free furnished accommodation, light, and water. Generous leave, with air passages paid for self and family.

(2) A Lady GYNÆCOLOGIST, with an M.R.C.O.G. or evidence of an equivalent academic standard, to develop and run a combined Obstetrical and Gynæcological Department comprising about 50 beds. The applicant must be capable of carrying out major gynæcological operation. (Salary as for 1.)

(3) A RADIOLOGIST, with a higher qualification in radiology, to run the X-ray Departments of the State Hospital (250 Beds), of the State Sanatorium (300 Beds) and of the State Hospital Annexe (80 Beds, expanding); also to organise a Department of Radiotherapy. (Salary as for 1.)

(4) A Lady RADIOGRAPHER for work in certain of the departments mentioned in para. 3. Salary £1343–£90–£1793 p.a. (monthly Rs. 1500–100–2000) with free furnished accommodation, light, and water.

(5) A Lady PHYSIOTHERAPIST, to organise and run a Department of Physiotherapy in the State Hospital. (Pay as for 4.)

Applications should include a complete resume of the candidate's academic and professional career, a statement of age, of family responsibilities, and the names and addresses of 3 referees, to whom reference may be made by the Department of Health. The closing date for applications, which should be sent air mail, is 15th November.

EDINBURGH. CITY OF EDINBURGH. *Applications* are invited for the post of ASSISTANT SCHOOL MEDICAL OFFICER (Male or Female) in the Edinburgh School Health Service. Possession by applicants of the Diploma in Public *Health will be an added qualification. The salary scale is* £950–£1300 with placing according to experience in local authority service. The successful candidate will require to undergo a medical examination and to become a contributor to the Corporation superannuation scheme.

Applications, giving age, qualifications and experience and the names of 3 referees, to be sent to the Medical Officer of *Health, Johnston-terrace, Edinburgh, not later than 30th* October, 1954.

FLINTSHIRE COUNTY COUNCIL. (Population 145,100.) Applications are invited for the appointment of DEPUTY MEDICAL OFFICER OF HEALTH (Male) from duly qualified and registered medical practitioners holding the Diploma in Public Health or similar qualification. Salary £1450 p.a., rising *by annual increments of £50 to £1700 p.a., plus a car allowance.* The appointment is superannuable and the successful candidate will be required to satisfy a medical examination.

Form of application and further particulars can be obtained from the undersigned and applications should be returned not later than 1st November, 1954.

W. HUGH JONES, Clerk of the County Council.

County Buildings, Mold.

LAGOS TOWN COUNCIL, Nigeria. (a) Maternity and CHILD WELFARE OFFICER and (*b*) ASSISTANT MEDICAL OFFICER OF HEALTH required by the above Council. *Salary : (a)* £1290 for 1 year then £1350–£40–£1470–£1500 ; (*b*) £770–£40–£1500, plus (in each case) £100 a year staff pay and expatriation pay of (*a*) £270/ (*b*) £180, rising to £350 a year in each case. Point of entry depends on applicants' qualifications and experience. Free passages for Officer and wife. Assistance towards cost of children's passages or grant of up to £150 annually for their maintenance in United Kingdom. Liberal leave on full salary after each tour of 12–24 months. Outfit allowance up to £60 in certain cases. Candidates must be registered medical practitioners and for post (*a*) have had at least 5 years practical experience after qualifying. The duties of post (*a*) consist of Antenatal and Domiciliary Midwifery Service and in the child welfare clinics. The duties of post (*b*) consist mainly of the control of infectious diseases, health education, antenatal and child-welfare work. Opportunities will be provided for postgraduate training in public health work. In each case the duties are full time. They may also include such other duties as the Medical Officer of Health may allocate. Applicants must disclose whether they are related to any Councillor or Senior Officer of the Council. Canvassing will be treated as evidence that the applicants merits alone are insufficient to justify appointment.

Write to the Crown Agents, 4, Millbank, London S.W.1, enclosing at least 2 copies of recent testimonials. State age, name in block letters, full qualifications and experience and quote (*a*) M3A/34392/LD or (*b*) M3A/34355/LD.

WALSALL. COUNTY BOROUGH OF WALSALL. ASSISTANT MEDICAL OFFICER OF HEALTH. Applications are invited from qualified medical practitioners for the above post at a salary of £950 p.a., rising by annual increments of £50 to £1300 p.a. Possession of the D.P.H. or D.C.H. will be considered an advantage. Commencing salary according to qualifications and experience.

Further particulars and application forms may be obtained from me. W. STALEY BROOKES, Town Clerk.

Council House, Walsall.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy"

WANSTEAD, London, E.11. Applications invited for retirement VACANCY (urban—intermediate). List at present approximately 1300. Residence available, by purchase, from the retiring Doctor. Apply on Form E.C.16A before 30th October, 1954, to E. BERGDAHL, Clerk of the Council.

Essex Executive Council, 131/3, Fillebrook-road, Leytonstone, E.11.

BULKINGTON, WARWICKSHIRE. Applications are invited for VACANCY at Bulkington in the Bedworth Urban District. List approximately 1900. Intermediate area. Residence and surgery available for purchase. Applications on Form E.C.16A to reach the undersigned not later than 25th October, 1954.

R. V. NELLTHORP, Clerk, Warwickshire Executive Council.

15, Waterloo-place, Leamington Spa.

MID-DEVON. Applications are invited for Vacancy (rural and dispensing). List approximately 1300. Applications on Form E.C.16A should reach the undersigned not later than 30th October, 1954. Further particulars may be obtained on request. H. BELL,

Clerk of the Executive Council for Devon and Exeter.

46, Queen-street, Exeter.

Hospital Services : Non-Medical Appointments

DUBLIN. ST. LAURENCE'S HOSPITAL. The Board of Governors invite applications for the post of RECORDIST TECHNICIAN for the Electro-encephalographic Unit at the Hospital.

Further particulars as to salary and terms of employment may be obtained from the under-mentioned, to whom applications should be addressed on or before 15th November, 1954.

A. W. MACDERMOTT, Secretary and Superintendent.

Miscellaneous

To non-professional posts the Notification of Vacancies Order 1952 applies.

A Medical Officer is required for Rhokana Corporation *Mine Medical Service at Kitwe, Northern Rhodesia.* There is a vacancy for a Medical Officer with an advanced qualification in medicine, preferably one who has had experience as Registrar. He will work under the Chief Medical Officer in association with the Physician already employed by the Corporation. His duties will include the care of patients in the Corporation's hospitals under the direction of the Specialist Physician, the *holding of clinics and some general practice. He may also be* required to take charge of the midwifery carried out in the hospitals. The Corporation employs 10 medical practitioners inclusive of the above-mentioned. Salary is at the rate of *£1700 p.a., part of which is deemed to be in lieu of private* practice. A modern house of bungalow type will be available immediately at a nominal rental. Water is free and the charges for light are low. A motor-car is provided free for use within the Corporation's area. There is a contributory pension scheme and a bonus is payable which varies with the profits made and is at present in the vicinity of 60% of salary ; it is paid in *part at Christmas, on going on leave and in cash and a portion* is deposited as compulsory savings withdrawable only on termination of service. Leave at the rate of 51 days p.a. accumulative up to a maximum of 153 days. The Corporation pays the cost of the outward passage of successful applicant and wife and family.

Application forms can be obtained from RHOKANA CORPORATION LIMITED. *11, Old Jewry, London, E.C.2.*

Assistant Doctor required early January for Anglican Native Mission Hospital (Government supported). 100 Beds. Salary £626, including cost-of-living allowance for single Man or Woman. Extra £50 for married man.—Applications, with details of previous experience and references to Medical Superintendent. St. Barnabas Mission Hospital, Ntlaza, Umtata, C.P. South Africa.

Christmas Island, Indian Ocean. Applications are invited for the position of Medical Officer at Christmas Island, duties to commence January, 1955. Applicants should be British born. British University Degree. Term of agreement 3½ years. Salary £1050 sterling p.a. for first 21 months, £1100 second 21 months. Adjustable allowance £224 sterling p.a. Ocean passage provided. Half pay on voyage. Intermediate leave of 2 months at end of first 21 months, 3 months at end of contract. If re-engaged, home leave 6 months. Child allowances. Provident fund and medical benefits fund. Free housing, partial furnishing. Low income-tax. Climate healthy, living conditions good. Fully equipped hospital.

Applications in writing, giving full particulars of qualifications and copies of testimonials, to the London Manager, THE BRITISH PHOSPHATE COMMISSIONERS, 2, Grosvenor-gardens, London S.W.1.

Works Medical Officer. Wanted for important Engineering Group, Midlands, full-time Medical Officer to supervise health services. Salary to recognised scales.—Full details, age, qualifications, industrial or other experience: Address, No. 973, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

British Schools Exploring Society 1955 Expedition. Applications are invited for the posts of an Hon. Physician and an Hon. Surgeon for the 1955 Expedition to Newfoundland, Greenland or Iceland, leaving about 28th July and returning mid-September, 1955. The cost to each member will be in the neighbourhood of £200.—Applicants should apply as soon as possible to the Secretary, British Schools Exploring Society, c/o Royal Empire Society, Northumberland-avenue, W.C.2.

Hand-picked Secretaries, S.R.N. and otherwise.—Wigmore AGENCY FOR MEDICAL SECRETARIES, 67, Wigmore-street, W.1 (HUNter 9951 2 3).

Harley-street, W.1. Large, newly decorated, consulting-room. £325 p.a. inclusive—D. PINTO & Co., 15, Dover-street, W.1 (HYDe 2244).

Brighton, Sussex-square, overlooking gardens and sea. First-floor self-contained furnished balcony flat, also ground-floor flat.—LIPMAN, 9, Blomfield-court, W.9 (CUN 7128).

For Sale. McKesson Portable Anæsthetic Machine. Model L with full recording Nargraf head. Circle absorber and ether bottle. Oxygen, carbon dioxide and cyclopropane flow-meters, and yokes. All attachments. Case and stand cover. Good condition. Offers.—Address, No. 974, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

Austin. The new Cambridge A.40 and A.50 and all Show models. Limited number of orders now acceptable from proven essential users.—Application form, brochures, easy terms, from Austin House, 140/144, Golders Green-road, Golders Green, London, N.W.11.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Haematology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for post requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE, LTD., 98, Victoria-street, S.W.1 (Phone : VICtoria 0141), who are specialists in this kind of work.

Medical and scientific typewriting (including theses), French-English translation and précis.—Miss H. E. M. WELCH, S.R.N., S.C.M., 3, Tennyson-road, Bath, Somerset.

The British Journal of Medical Hypnotism. Quarterly. £1 1s. p.a.—Orders to the Publishers, 4, Victoria-terrace, Hove, 3, Sussex.

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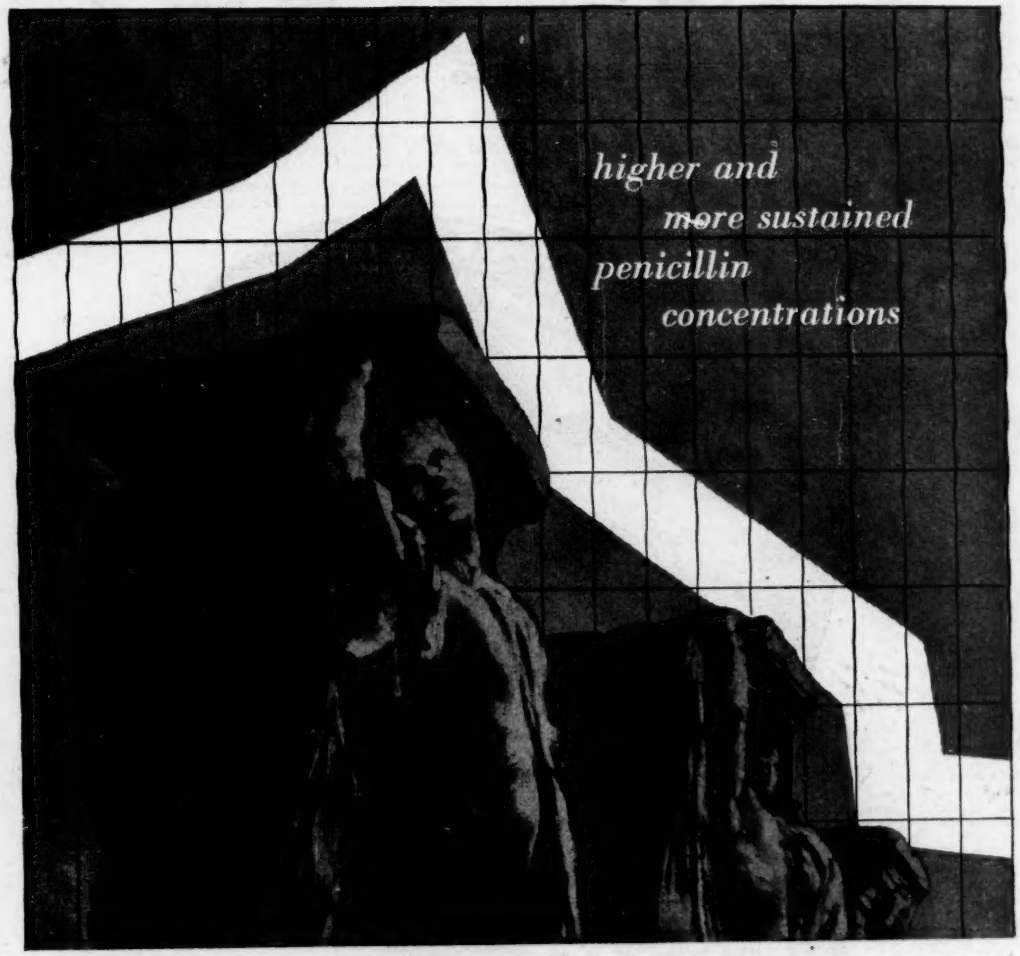

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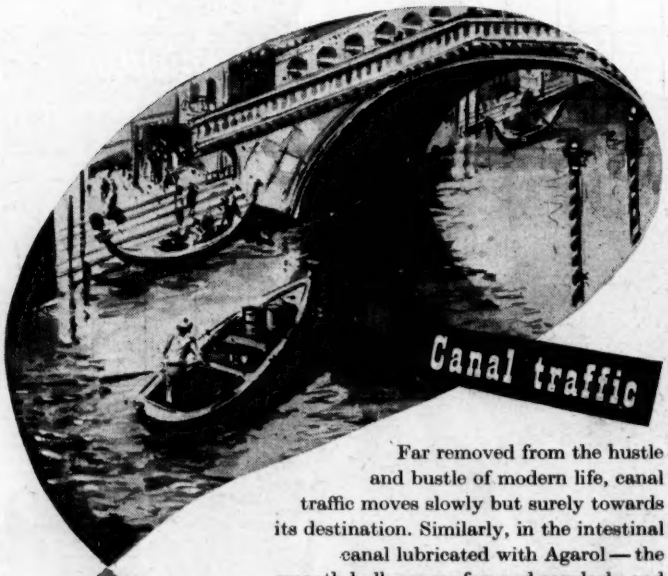

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